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## Carcinoma of the Skin: Influence of Dosage on the Success of Treatment<sup>1</sup>

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THIS STUDY was undertaken in an attempt to evaluate the effect that a given number of roentgens, delivered to a carcinoma of the skin, had upon the success or failure of treatment. By comparing the results in large groups of lesions each given a different dosage, it was hoped that an optimum dose might become apparent. With the establishment of such an optimum dose, the existing confusion as to the proper roentgen dosage for skin cancer should be considerably lessened, and a standard of treatment more uniform throughout the country might be accepted.

It is a well recognized fact that few patients die of carcinoma of the skin, and also that recurrence, even after months and sometimes years of apparent cure, is not uncommon. A study based on three- and five-year cures following treatment of these lesions is never entirely satisfactory, largely because approximately 25 per cent of the patients affected by skin

cancer, due to their age, die of intercurrent disease within five years from the time of treatment. Also, many of these patients are too feeble for the enforcement of routine follow-up, and on this account many real five-year cures may be listed as lost.<sup>4</sup>

In the present discussion, the word "failure" will be used arbitrarily to indicate both those cases in which the lesions were not immediately destroyed by a given treatment and those in which there was later (months or years after treatment) recurrence. (Actually, most of the lesions referred to as failures were subsequently destroyed or controlled by irradiation or surgery.) In only 3 of the entire group studied could the carcinoma of the skin be considered as a contributing cause of death. Undoubtedly, a certain number of lesions classified as successfully treated recurred without our knowledge, or may still recur. Any such inaccuracies, however, should not influence the

<sup>1</sup> From the Department of Radiology, Massachusetts General Hospital, Boston 14, Mass. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

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<sup>4</sup> An analysis, by the methods of Warren *et al.* (2, 3) and Magnusson (1), of the known three-year and five-year cures in this series will be discussed in a later paper.

comparative results, since they should apply more or less equally to all groups regardless of the roentgen dosage used.

Approximately 1,500 carcinomas of the skin were reviewed for the purposes of this study. (Lesions of the mucocutaneous junctions are not included.) They were found on 1,300 patients. The lesions were taken in the order in which they appeared on the hospital files between the years 1930 and 1944 inclusive. The group is a selected one only to the extent that lesions which had received treatment elsewhere, prior to admission to the Massachusetts General Hospital, were discarded. This was done because the purpose of the study was to evaluate the various methods of treatment used at this hospital. Ten hundred and thirty-five lesions were irradiated with x-ray and 387 were treated surgically. Histologic examination in 630 of the total group showed epidermoid carcinoma in 183 and basal-cell carcinoma in 447. In the remaining cases, treatment was given without histologic confirmation because the clinical appearance was characteristic of carcinoma of the skin. A few benign lesions may have been included in the latter group, due to error in judgment, but such diagnostic errors would be fairly equally distributed throughout the different dosage groups and should not affect the proportional results. Seventy-eight of the 129 so-called failures in the irradiated group were proved by biopsy; 61 (78 per cent) were basal-cell and 17 (22 per cent) epidermoid carcinomas.

No lesion was included in the analytic study in which the follow-up had been less than one year; 63 of the initial group were discarded on this account. Sixty-eight per cent were followed two years or more; 25 per cent five years or longer.

The dose of radiation varied from 1,200 r to 6,000 r measured in air. In 89 per cent of the irradiated group, radiation was given in a single massive dose, while in the remainder it was fractionated over a period of from one to three weeks. Of the 893 lesions receiving a single massive treatment, 54 per cent were irradiated with

200 kv., 0.25 mm. Cu filter, 20 cm. S.T.D., half value layer 0.6 mm. Cu, while the other 46 per cent were treated with 100 kv., the half-value layer of which was 1 mm. Al.

The solid line of Figure 1 is a curve plotted on the percentage of failures resulting in the various dosage groups, to each of which a different number of roentgens were administered in a single dose. On the supposition that such a graph forms a fair comparison of the success of a given treatment, the fewest number of roentgens used at the most favorable point of the curve is accepted as a so-called optimum dose. Among the 893 lesions analyzed, there were 101 failures. The contour of the curve indicates a very definite improvement in the results of treatment as the dosage was increased up to approximately 2,700 r. It does not suggest that any improvement in the results followed the increase in dosage from 2,700 r to 4,000 r. It seems reasonable therefore, to accept 2,700 r as the optimum number of roentgens to be administered in the treatment of cancer of the skin by this method. No claim is made that the universal application of this amount of treatment will produce 95 per cent cures, but it is evident that in the treatment of nearly 900 lesions, 2,700 r was as effective in destroying the carcinoma as any of the dosages used. It has the added advantage of carrying with it a lesser likelihood of leading to post-irradiation complications than larger doses.

It is appreciated that the number of roentgens to be given to an epithelioma should not be determined entirely in terms of the surface dose, but that the number delivered to the deepest portion of a lesion must be taken into consideration as well (4). In this study, the doses mentioned indicate the number of roentgens delivered to the skin and, by and large, apply to lesions of average thickness. Every radiation therapist should routinely estimate the depth dose so that the amount of radiation delivered at the deepest portion of a tumor can be kept fairly constant by increasing the surface dose in proportion to the depth of the tumor.

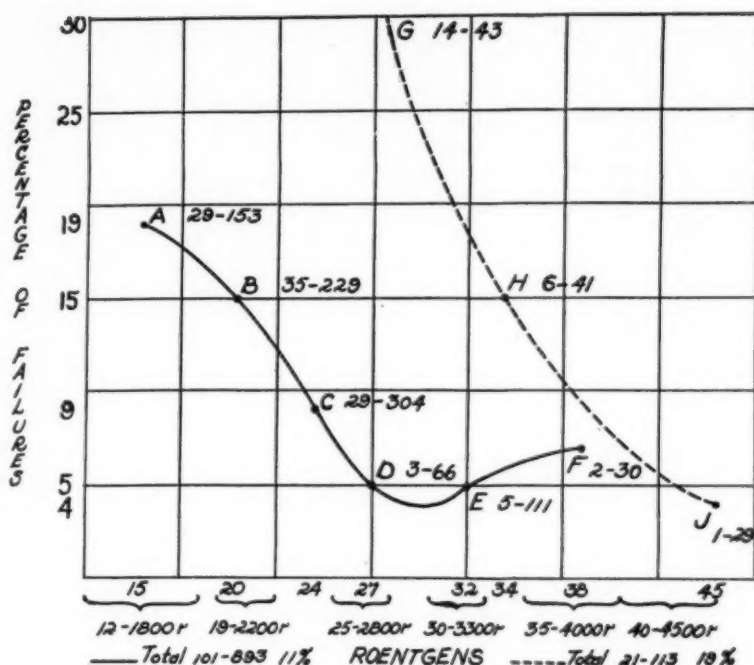


Fig. 1. Comparative results of treatment of cutaneous cancer. Solid line represents group treated with massive single-dose irradiation (893 lesions). Broken line represents those treated with multiple doses, fractionated within one week (113 lesions)

- A. 29 failures (19%) in 153 lesions given 1,200-1,800 r.  
 B. 35 failures (15%) in 229 lesions given 1,900-2,200 r.  
 C. 29 failures (9%) in 304 lesions given 2,400 r.  
 D. 3 failures (5%) in 66 lesions given 2,500-2,800 r.  
 E. 5 failures (5%) in 111 lesions given 3,000-3,300 r.  
 F. 2 failures (7%) in 30 lesions given 3,500-4,000 r.  
 G (fractionated). 14 failures (32%) in 43 lesions.  
 H (fractionated). 6 failures (15%) in 41 lesions.  
 J (fractionated). 1 failure (4%) in 29 lesions, dosage  $\approx$  4,500 r.

Among the total 1,035 lesions treated with radiation, there were 26 in which radiation ulceration developed several months to several years after complete healing. All 26 ulcerations occurred in lesions that had received a single treatment or a single course of treatments. In 12, the dose had been 3,000 r or less; in 11, between 3,000 r and 4,000 r; and only 3 lesions had received over 4,000 r. Although the size of a given cancer of the skin must always be considered in estimating the probability of the development of a late radiation ulcer, it must be borne in mind that this complication may also follow the treatment of a relatively small lesion. Of the 26 radiation

ulcers, 10 occurred after treatment of lesions 1 cm. or less in diameter; 12 in lesions between 1 and 2 cm., and only 4 in lesions larger than 2 cm. It is well known that treatments repeated over a period of months or years greatly increase the likelihood of the development of radiation ulceration, but it would seem that, in the past, proper emphasis has not been given to the danger of radiation ulcer resulting from the irradiation of a small lesion to which but a single treatment (or a single course of treatment) has been administered. During the past fifteen years, approximately one-third of the total number of radiation ulcers associated with the treatment of skin carcinoma at this

hospital have developed following a single treatment (or course of treatments). An interesting observation made during the study of the 26 radiation ulcers was that all but 2 developed in the scar of a lesion that had been treated with the shorter wave length, half value layer 0.6 mm. Cu.<sup>5</sup>

TABLE I: COMPARATIVE FAILURES WITH FRACTIONATED TREATMENT OF SKIN CANCER (Total delivered within one week)

Dosage Roentgens	Number Cases	Failures
2400-3000	43	14(33%)
3200-3600	41	6(15%)
3700-4500	29	1(4%)

Table I compares the results of different dosages in 113 lesions irradiated by the fractionated method, the treatments being delivered during the period of one week. In the group given 3,700 r to 4,500 r, the majority of lesions received 4,500 r.

The data shown in Table I appear also on Figure 1, being represented by the dotted line. Comparison of the two curves on Figure 1 makes it evident that between 3,200 r and 3,600 r, fractionated within one week's time, must be delivered in order to obtain results as good as those obtained with 1,900 r to 2,200 r given in a single treatment. Approximately 4,500 r in multiple doses within one week must be given to secure results equivalent to those resulting from a single dose of 2,700 r. In other words, the optimum dosage for fractionated treatment (within one week) is about 4,500 r and corresponds to 2,700 r as the optimum for the single-dose method. On the other hand, the number of lesions treated by the former method is too small (113) to warrant as unqualified acceptance of this standard as in the case of the single dose method. The suggested optimum dosage of 4,500 r, however, corresponds fairly closely with the dosage recommended by other large clinics with considerable experience in the fractionated form of irradiation.

From a practical point of view, treat-

<sup>5</sup> A more complete discussion of radiation ulcers will be presented in a subsequent paper.

TABLE II: COMPARISON OF FAILURES IN SKIN CANCER WITH DIFFERENT METHODS OF TREATMENT

Type of Treatment	Number Cases	Failures
Single 200 kv.*	504	63(13%)
Single 100 kv.†	389	38(10%)
Multiple 200 kv.*	125	27(22%)
Multiple 100 kv.†	17	1(6%)
Total Irradiated	1,035	129(12%)
Treated Surgically	387	47(12%)
ALL METHODS	1,422	176(12%)

\* H.v.l. 0.6 Cu.

† H.v.l. 1.0 Al.

ment of a skin cancer with fractionated doses has one distinct advantage, in that it minimizes the seriousness of a technical error if one should occur. It is debatable, however, whether this advantage outweighs the economic saving which the single-dose method offers both to the patient and the busy clinic. The validity of the frequent statement that treatment of a cutaneous carcinoma should be fractionated so that the skin reaction may be lessened is questionable if the radiation is delivered within one week and the doses are comparable, that is, 4,500 r given by the former method and 2,700 r in a single treatment.

Table II shows the over-all results in the entire group studied, analyzed according to the type of treatment, without regard to the dosage used. It will be noted that the incidence of failures is the same in the group treated surgically and the group given roentgen radiation. In the latter group, dosage is obviously not the sole factor determining the result of a given treatment. An error in judgment in the estimation of the size of the subcutaneous portion of a lesion will result in failure in spite of adequate dosage to the irradiated portion of the tumor. An occasional failure may be due to the inability of a patient to remain precisely positioned throughout the entire period of treatment. In a few instances, the lesion may fail to respond even to tremendous amounts of radiation because of the actual radio-resistance of the tumor itself. Furthermore, as has been mentioned, the size of the lesion may influence the result of treatment.



Table III presents a breakdown of all the irradiated lesions included in this study from the point of view of the incidence of failure associated with the size of the lesion. In lesions of 2 cm. diameter or over, failures were twice as frequent as in those of 1 cm. or less. This fact, however, does not prove that the incidence of failure is always twice as great when the treated lesion is a large one. Table III does not take into consideration the dosage or the method of treatment used, and errors in either of these two factors may have been just as responsible for failure as the size of the lesion.

There is a tendency among radiologists to "think twice and then reconsider a second time" (and rightly so) before giving to a large area the same dose that would readily be given to a small one. On this principle, many large lesions may fail to respond to irradiation because of underdosage. In this clinic, the trend has been to use fractionated doses in the treatment of large lesions because of the common belief that by this method a larger dose could be delivered more safely and with less discomfort to the patient. On the assumption that 4,500 r in fractionated doses delivered within one week is the optimum dose, it is apparent from Table I that all but one of the failures received less than this optimum dose. In the treatment of large skin carcinomas, the point to be stressed is that the therapist should decide before treating whether or not it is reasonably safe to attempt to destroy the lesion with the dose that has a fair chance of doing so. If it is decided that destruction of the cancer by irradiation should not be attempted, surgical removal should be seriously considered.

If an optimum radiation dosage, which would give a 90 or 95 per cent cure prognosis, could be established, the therapist might well be content. It seems inevitable that 100 per cent cures can seldom be attained; error in judgment in estimating the size of the field to be irradiated, as well as technical errors, will probably always cause a few failures per hundred.

TABLE III: INCIDENCE OF FAILURES IN SKIN CANCER ACCORDING TO SIZE OF LESION

	Total	Diameter (centimeters) of Lesion		
		1 or less	1 to 2	2 or more
Number irradiated	1,035	644	305	86
Number failures	129	68	42	19
Per cent failures	12	11	14	22

Increase in the number of roentgens up to tremendous doses, such as 6,000 to 10,000 r, will not eliminate this small percentage of failures. The use of such doses would be justified only if it resulted in a significant decrease in the number of failures. If this is not accomplished, the obvious optimum dose is the lower of two doses giving essentially the same chance of cure, since the lower dose leaves the irradiated area much less liable to post-irradiation complications.

Presentation of the results of treatment based on so-called failures rather than on the curability of the lesion is misleading to a certain extent. For a fair evaluation of the various methods of treatment used, however, it has seemed more reliable, since one is dealing with patients whose ages alone predispose them to death from intercurrent disease within a relatively short time after treatment. A review of the 129 failures in the group treated by x-ray is of interest when the cases are divided according to the time after treatment that failure was noted. Within six months after treatment, 64 per cent of the failures were evident; 15 per cent were recognized during the second six months; 12 per cent between twelve and twenty-four months after treatment; and only 9 per cent occurred in lesions that had been cured for two years or more.

#### SUMMARY

Tabulation of the results of the single massive dose method of irradiation in carcinoma of the skin, over the range of the various doses used, showed that 1,200 r to 1,800 r gave only an 81 per cent chance of destroying the lesion. The administration of 1,900 r to 2,200 r did not offer bet-

ter than an 85 per cent chance, while the delivery of 2,400 r might raise the expectancy to 91 per cent. A constructed curve showed that a lesion was as likely to be destroyed with a 2,500 r to 2,800 r range as with the delivery of 4,000 r. In the group of cases studied, therefore, approximately 2,700 r may be considered the optimum dose, since it produced as satisfactory results as higher dosages and at the same time might be expected to leave the irradiated area in better condition.

Comparison of results obtained by multiple treatments within the period of one week and by the massive single-dose method indicates that 3,200 r to 3,600 r must be delivered by the former method to produce the same results as were obtained by 1,900 r to 2,200 r by the latter. Approximately 4,500 r delivered in multiple treatments within one week produced essentially the same results as 2,700 r given at one time. This dosage, 4,500 r, is suggested, therefore, as the optimum dose to be delivered to a carcinoma of the skin when the fractionated method (within one week) is to be used.

Twenty-six late radiation ulcerations were observed following the treatment of lesions which were not extensive in size and which did not receive more than a single treatment, or a single course of treatments. Ninety-two per cent developed following the use of heavily filtered radiation (half value layer 0.6 mm. Cu), while only 61 per cent of the *total* lesions were so treated. The roentgen dosage responsible for these ulcers would not be considered excessive by most standards. The fact that late radiation ulceration does develop following the treatment of a small lesion with a relatively small amount of radiation makes questionable the routine treatment of all skin cancers with an excessive dose of radiation in the false hope of obtaining perfect results. The chance of destroying the lesion with a much smaller amount is essentially as good as with the tremendous dosage, and the danger of subsequent complication to the patient is much less. If necessary, the few lesions that may recur

because of inadequate dosage may be successfully treated later by surgical removal.

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#### DISCUSSION

**Frederick W. O'Brien, M.D.** (Boston, Mass.): I think Dr. Hale is to be congratulated for having done a nice piece of work, and perhaps he will carry it even further. I would be particularly interested in knowing the relationship of the size of the field to his results; that is, if in all these cases ports of only 1 cm. or 2 cm. were used. While I believe he has shown that the radiation quality is probably not too important, I am sure the size of the field might very definitely have some significance in the types of therapy that he referred to, 100 and 200 kv.

I was also interested in the end-results—about 12 per cent of failures with surgery or with irradiation. Most of us have thought for a good many years it did not make much difference whether one used surgery or x-ray in these cases; the results were about the same.

Dr. Hale has confirmation in recent literature for his point regarding fractionated doses. Poulsen, in *Acta Radiologica*, showed very definitely that the biological effect is less with fractionated radiation in carcinoma than it is with continuous therapy.

I do not know whether the intensity rate would be important in these very small lesions, or not; I think it might well be in the larger lesions.

**Henry J. Ullmann, M.D.** (Santa Barbara, Calif.): Before this Society a few years ago, in this hotel, I reported what I call late radiation breakdown in 3.6 per cent of cancers of the skin that I had treated. These lesions all exceeded 1 cm. in diameter. Most of them were 2 to 2.5 cm. The breakdowns all occurred between one and a half and two years following irradiation. The

doses were in all instances divided. All my doses are given in one of two ways, depending upon the distance at which the patient lives—two one week apart or three separated by intervals of a day; that is, the entire treatment is given within one week, whether it is divided into three doses or two.

Some of these breakdowns occur without any exciting cause. To illustrate, some years ago I treated a carcinoma of the lower lip near the left angle of the mouth, and several years later an exactly similar lesion appeared on the opposite side. This second lesion was given the same dose of radiation to an area of the same size as the first. About a year and a half later there was a radiation breakdown in the second lesion, though the first had never caused any trouble. The patient was positive that he had a recurrence and wanted surgery. The surgeon did a biopsy and found chronic inflammation, which was well in the usual less than three months' time.

Sunburn may start these breakdowns. I treated a lesion on the crown of the head with radium. A couple of years later the patient, who was bald, forgot to wear his hat and acquired a good sunburn. The center of the lesion broke down and healed in the usual way in about two and a half months. An interesting thing to me is that these breakdowns usually heal leaving less scar than the original lesion, and that they all heal within three months. The treatment I have used consists in application of an ointment known as Veracal, which is 50 per cent aloes vera jelly in an oil-and-water emulsion base. This is applied in the usual manner, but under wax paper, and changed as needed, and I see the patients often enough to keep them from worrying too much about a recurrence, which is what they usually think has happened.

I am interested in seeing what my future results will be, because I have just changed from a half-value layer of approximately 0.8 mm. Al to a half value of 1.8 mm. Al. That is the half-value layer I get at 100 kv. with the inherent filtration in the machine I am now using, which is supposed to be equivalent to 1 mm. Al. I have treated a number of lesions of 5 cm. or more with high-voltage, copper-filtered radiation, a half-value layer in copper of 1.15. I split the dose into 250 to 300 r a day, measured on the skin, as all my doses with high voltage are controlled with an integrator, and I usually give a total of 4,500 to 5,000 r measured in this way. So far, the only breakdown I have had following this treatment was on a hand, following severe trauma, and several of these patients were treated a number of years ago.

**Arthur W. Erskine, M.D.** (Cedar Rapids, Iowa): As Dr. O'Brien has suggested, I think it would be interesting if the number of failures were plotted against the size of the lesion and the age of the patient.

I was a little surprised at what Dr. Ullmann said about these radiation ulcers healing without any trouble. We see them on the lip in elderly patients—sixty years old—and they do not heal very well, and we have them excised.

I am one of those who believe that anybody's method is good. We used to hear George Grier say that all epitheliomas should be treated with unfiltered x-rays. On the other hand, when we first started to use 200 kv. copper-filtered rays somebody would tell us how much better that method was. It seems to me that quality has very little to do with our number of failures. I made a study at one time of several hundred epitheliomas and, because there were so many of them, I confined my remarks to the failures and tried to analyze the reasons for them. There were many—the stage of the disease, the age of the patient, the degree of malignancy, and a number of others, including over-treatment and under-treatment. I found that for each patient to whom I wished I had not given so much there were nine patients to whom I wished I had given more treatment.

**Dr. Hale (closing):** I believe I can best answer Dr. O'Brien's question by giving the comparative results obtained in the treatment of the large and small lesions. In the group of lesions which were approximately 1 cm. in diameter, there were 11 per cent failures; in the group which were approximately 2 cm. in diameter, there were 14 per cent failures, while in the group measuring 2.5 cm. or more, there were 22 per cent failures. Sixty-two per cent of all the lesions fell into the 1 cm. group; 30 per cent fell into the 2 cm. group, while only 8 per cent exceeded 2.5 cm.

One's first impression of these results—22 per cent failures for the larger lesions *versus* 11 per cent for the small lesions—would be that it is considerably more difficult to destroy the larger lesions. I do not believe, however, that the difference is as great as these figures would suggest since, as you may recall, we were inclined to treat the larger lesions with a fractionated type of therapy and, if our constructive minimum-optimum dose is roughly correct, they were obviously under-treated. It is my impression that the high percentage of failures in the treatment of larger lesions can be accounted for, in part at least, by the relatively smaller effective dose which they received.

## Simultaneous Cross-Radiation<sup>1</sup>

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**I**N A PAPER published in February 1938, the advantages of simultaneous cross-radiation were discussed by the writer and a description was given of an apparatus built by the Kelley-Koett Manufacturing Co. for that specific purpose. Eight years of constant use have shown that this method of irradiation has decided advantages, and case reports are submitted to substantiate this claim.

Theoretically, the ideal method of irradiating a tumor would be to give a saturation dose and then repeated smaller doses at frequent intervals, keeping the saturation point constant during the entire cycle of malignant cell mitosis. Practically, this can be accomplished in superficial lesions, but in deep-seated tumors the danger to adjacent healthy tissues constitutes an obstacle. This difficulty is solved in part by changing the position of the patient, or the ports of entry, or both, in such a manner that the roentgen-ray beams cross their own path at a certain depth below the skin, producing a radiation effect of greater intensity at tumor depth and distributing the superficial dose over a larger area.

Many radiologists believe that failure to obtain uniform good results in irradiating deep-seated tumors is due to the fact that one cannot administer a carcinocidal dose quickly enough without injury to surrounding normal tissue. The time which elapses between exposures induces failure, for it is well known that the radiation effect diminishes proportionally as much as 50 per cent every twenty-four hours. Simultaneous cross-radiation is based on the principle of administering quickly large doses of radiation at depth and distributing the superficial dose over large areas through a great number of

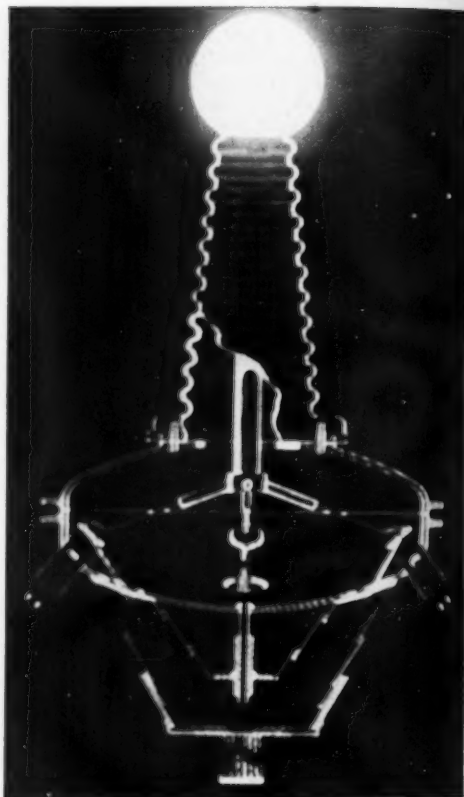


Fig. 1. Section of the original Loebell simultaneous cross-radiation therapy tube (fourth target out of view).

ports at the same time. The advantage lies in the fact that a carcinocidal dose can be administered to a neoplasm while the tumor bed, receiving a non-lethal dose, recovers quickly and is capable of replacing destroyed malignant structures with benign fibrous tissue, blood vessels, and the like. Lymphoid tissue and young metastatic islands outside of the tumor area, being more radiosensitive, are also gravely affected. Large daily doses applied di-

<sup>1</sup> Read by title at the Twenty-ninth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-2, 1943. Submitted for publication in October 1946.





Fig. 2. Multiple port apparatus in use at the Bethesda Hospital (Zanesville, Ohio).

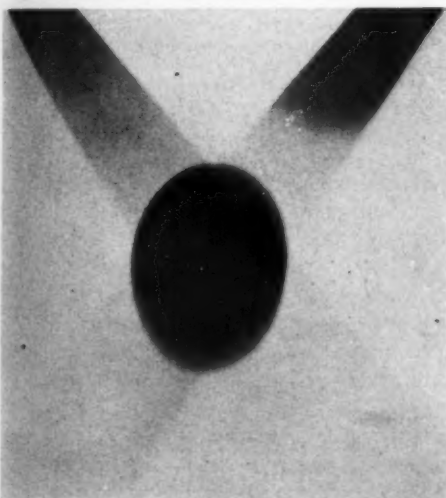


Fig. 3. Film placed perpendicularly through center of opposing ports of simultaneous cross-radiation apparatus. Note density of beams at the top of the phantom, gradually diminishing and again increasing at the area of cross-radiation. The oval shadow is produced by beams entering at right angles. Also note the fading of x-ray beams beyond area of cross-radiation.

rectly to a neoplasm tend to keep the saturation point constant and the result compares favorably with that obtained in superficial therapy.

A carcinocidal dose can be administered with simultaneous irradiation at any depth. This is made possible by the great number

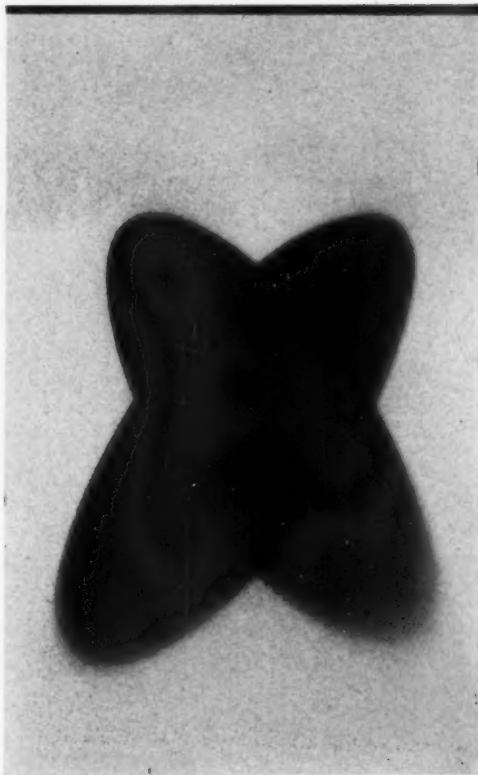


Fig. 4. Film placed perpendicularly half way between the four ports. Line represents surface of phantom (or skin area).

of ports of entry (32 or more) through which x-ray beams are brought to converge on any specific area, producing a homogeneous radiation effect. Even in lesions of lesser depth, such as cancer of the breast, there is an advantage in cross-radiation, since the x-ray beams are tangential to the underlying structures and injuries to the lungs, pleura, and the like, such as often occur with perpendicular x-ray beams, are avoided.

Due to technical difficulties encountered with vacuum pumps, the original model described in the first published report was replaced by the present one, which has been in use since 1939. It consists of a shock-proof, oil-filled, lead-lined steel tank containing a 200-kv. transformer surrounded by four balanced x-ray tubes. The oil is cooled by a continuous flow of tap water

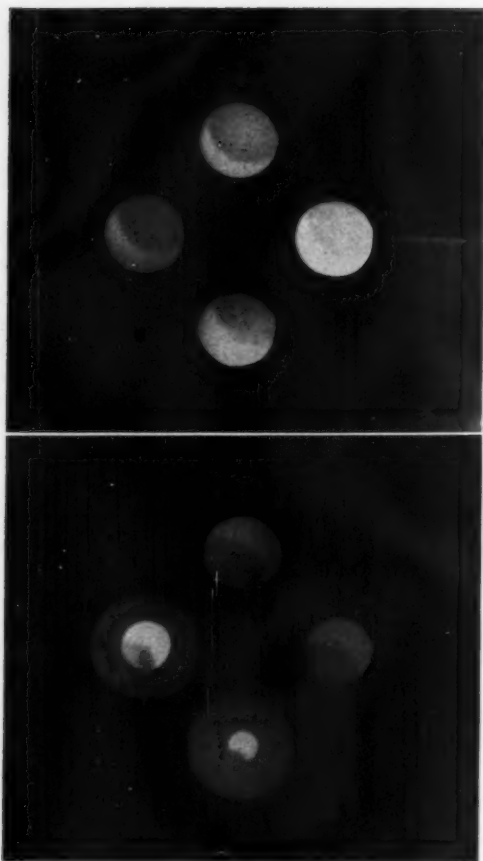


Fig. 5. Lead diaphragm encased in steel, showing all four ports. In the lower view the size of the fields is reduced by the insertion of lead rings of various sizes.

through copper coils which are attached to the tank's inner wall. Since the roentgen rays are confined within heavy steel and lead enclosures, neither primary nor secondary radiation can escape except through the portals in the diaphragm, which are in direct contact with the skin, and, since filtration occurs at the skin, very little secondary radiation is transmitted to the patient. The grounded tube affords protection both to patient and operator.

Changing the position of the openings in the regulating diaphragm makes possible the dovetailing of roentgen-ray beams, which may be concentrated upon a tumor with little cross-radiation outside of the neoplasm. By varying the position of the

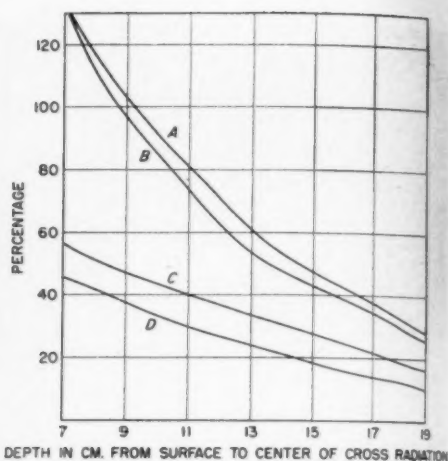


Fig. 6. Percentage of skin dose delivered to tumor depth with multiple target apparatus and with conventional target tube.

A. Multiple target, 200 kv., 5 ma. (each target), 2 mm. Cu + 1 mm. Al.

B. Multiple target, 200 kv., 5 ma. (each target), 1 mm. Cu + 1 mm. Al.

C. Conventional single target, 220 kv., 15 ma., Thoraeus filter, equivalent to 2 mm. Cu.

D. Conventional single target, 220 kv., 15 ma., 1 mm. Cu + 1 mm. Al.

All curves were obtained through the same phantom and the same surface areas.

portals or the position of the patient, one can reach a definite and identical depth through from 32 to 40 ports of entry with little cross-radiation elsewhere.

Each tube filament is regulated individually at the control cabinet, so that the output at all ports can be calibrated uniformly. Targets are arranged at 60-degree angles. A series of heavy lead diaphragms, encased in sheet steel, each of which has four apertures, is calculated to allow the x-ray beams to cross at different depth levels of 1 cm. variations below the surface of the skin. The relative position of the openings in the diaphragm determines the level of cross-radiation. The closer the openings are to the center of the diaphragm, the nearer to the surface the rays will cross; the farther the apertures are apart, the deeper the site at which the rays meet.

The target-skin distance is fixed and unchangeable and depends, under all circumstances, upon the distance between the center of the tumor and the skin. On each

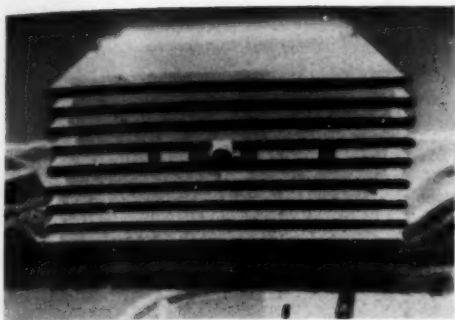


Fig. 7. Plaster-masonite phantom, with ionization chamber in position.

diaphragm is indicated the thickness and kind of filter and the exact target-skin distance. In the center of the diaphragm is a marker which indicates a perpendicular line to the exact center of cross-radiation at various levels.

Because of the variation in the size of x-ray beams at different levels, apertures in the several diaphragms differ slightly in size, so that the area of cross-radiation in the present model is exactly 100 sq. cm. at all levels. The size of the area can, however, be regulated by a series of lead ring inserts placed in each opening. In irradiating a pituitary gland, larynx, or other small area, intense irradiation can be carried out without exposing too much of the surrounding normal tissue.

The important procedure of locating a lesion cannot be delegated to a technician or to an inexperienced assistant, but must be carried out by the radiotherapist himself. The exact distance from the center of the tumor to the skin surface in the various positions (*i.e.*, anteroposterior, postero-anterior, right and left lateral, etc.) having been determined, measurements are taken from anatomical points such as the ensiform process, symphysis pubis, iliac spines, umbilicus, and the like, and are marked on the surface. Positioning is thus simple and accurate. After determination of the total dose and the daily depth dose, any trained technician can carry out the treatment easily and precisely. The patient is placed tightly against the diaphragm with

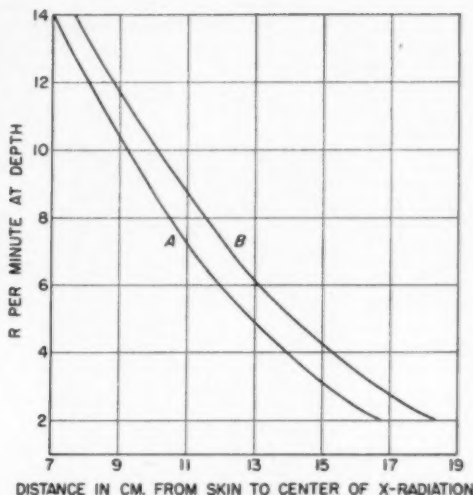


Fig. 8. Almost exactly parallel curves obtained in measurements at depth through living tissues (A) and through plaster-masonite phantom (B). Cross-radiation: 200 kv., 1 mm. Cu + 1 mm. Al.

the center of the mass to be treated (marked on the skin) located directly under the center indicator. A diaphragm with the proper depth designation is selected, and the desired filter is inserted above the diaphragm.

In calibrating depth dosage at the level of cross-radiation, I constructed a practical phantom by using alternate layers of plaster board (1 cm. thick) and masonite (1.2 cm. thick). Curves thus obtained have been found to parallel almost exactly measurements taken on a series of patients of varying sizes and thicknesses. The phantom is made up of loose 18 × 18-inch square boards, one pair having a slot to accommodate the ionization chamber. On the top board is marked the exact position of the chamber, which should always be in the center of cross-radiation when the proper diaphragm is used. Exception to the dosage chart is made in the treatment of chest lesions because of the decreased density in lung tissue.

By removing the diaphragms from the apparatus, whole body radiation can be accomplished in leukemias and other conditions where telerradiation or spray radiation has been found to be of value.

MULTIPLE PORT CROSS-RADIATION WITH 200 KV. CALIBRATION BY PHANTOM SHOWING DOSAGE AT VARIOUS DEPTHS AND PERCENTAGE DEPTH DOSE AS COMPARED TO SKIN DOSE

Distance		Filtration			
Target to Field, cm.	Skin to Field, cm.	2 mm. Cu + 1 mm. Al Depth Dosage		1 mm. Cu + 1 mm. Al Depth Dosage	
		r per min.*	% of skin dose	r per min.*	% of skin dose
41.9	At surface	7	100	11	100
48.9	At 7 cm.	9.5	135	14.5	131
49.6	8	8	114	12.5	109
50.5	9	7.25	103	11	100
51.1	10	6.5	93	9.5	86.75
52	11	5.75	82.14	8	72.75
52.6	12	5	71.4	6.75	61.8
53.5	13	4.25	60.7	5.75	52.75
54.1	14	3.75	53.6	5.25	47.75
55	15	3.25	46.4	4.75	44
55.8	16	3	42.85	4.25	38.65
56.5	17	2.75	39.28	3.75	34.5
57.2	18	2.25	32.14	3.25	29
58.1	19	2	28.57	3	27.5

\* With back-scatter.

The following reports are presented as illustrative of results obtained by simultaneous cross-radiation in a variety of cases of advanced cancer.

#### CASE REPORTS

The first case illustrates the advantages and almost dramatic effects of large depth doses of x-rays given daily.

CASE I: Charles P., 11 years old, was sent to the hospital on March 17, 1946, for diagnosis. He was cyanotic and unable to lie down because of shortness of breath. A chest film showed a large mass in the mediastinum, filling about one-half of the chest cavity. The temperature was 100°, the pulse 90, the blood count essentially normal, and urinalysis negative. Cervical, axillary, and inguinal lymph nodes were palpable but small.

A tentative diagnosis of Hodgkin's disease was made and irradiation was begun on March 19. A calculated tumor dose of 200 r was administered daily for ten days, totalling 2,000 r. The skin dosage was 165 r at each port, measured in air with back-scatter, totalling 660 r each day, or 6,600 r for the ten treatments.

During the night following the first treatment the patient's condition was critical. He showed some improvement the next day, and continued to do so. On the fifth day he was able to lie down, and on the tenth day he was out of bed, walking and apparently in normal health. Physical examination showed no symptoms of respiratory embarrassment. A roent-

genogram taken the same day revealed a complete disappearance of the mass.

Two months later the patient was brought back to the hospital, a very sick child. A chest film showed no recurrence of the tumor, but the blood picture had undergone a marked change, showing 3,000,000 red cells and 240,000 white cells, mostly lymphocytes, with a great number of lymphoblasts. A definite diagnosis of leukosarcoma was now made. Blood transfusions and other supportive measures were without effect, and death ensued two weeks later. The white cell count on day of death was 400,000.

CASE II: Mrs. B. G., white, age 68, had discovered a lump in her left breast eight months previously but did not seek medical aid until she felt a painful mass in the left axilla. Meanwhile, her breast became ulcerated. She consulted a surgeon, who thought that the lesion was beyond surgical help and referred her for palliative x-ray therapy.

Simultaneous cross-radiation was given from July 18, to Aug. 5, 1944, with a daily average of 300 r, as determined for the center of the tumor. The total dose was 4,800 r at depth over a period of three weeks, omitting Sundays. Radiation was given through four ports with an average daily skin dose of 880 r, covering the axilla, supraclavicular and infraclavicular areas, and a total dose of 12,500 r. Radiation factors were 200 kv., 20 ma., 1.0 mm Cu + 1.0 mm. Al filtration, 50 cm. target-skin distance. The apertures were 12 cm. in diameter; the average time per treatment was 22 minutes. A mild epithelitis developed which cleared completely within three weeks.



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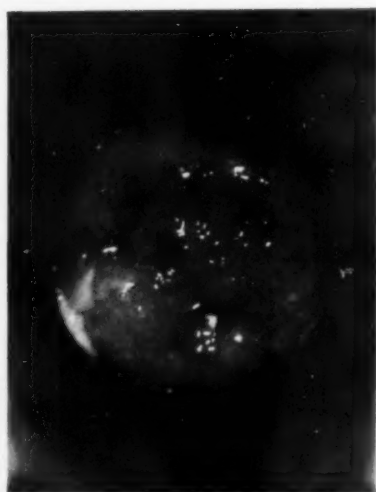
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Case II: July 18, 1944.



Case II: October 20, 1944.



Case V: Aug. 5, 1942.



Case V: Nov. 6, 1942.



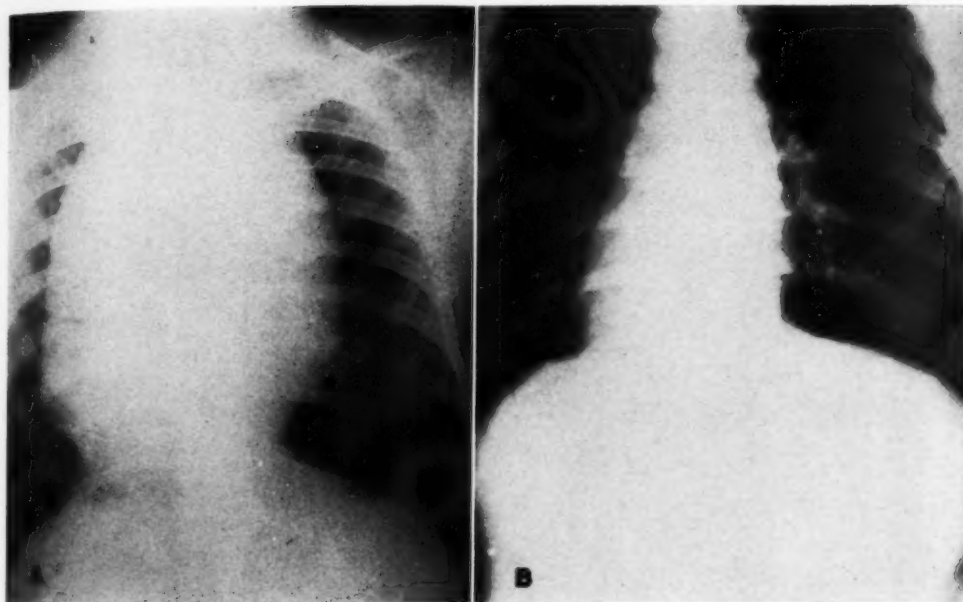


Fig. 9. Case I: Mediastinal tumor (leukosarcoma). A. Roentgenogram made March 17. B. Roentgenogram made March 29, ten days after irradiation was begun.

There is no evidence of recurrence at present, although the time elapsed is too short to predict the outcome. The patient feels perfectly well and is able to do her housework. The axillary nodes have receded and are no longer palpable. (See color plate.)

**CASE III:** Miss N. E., white, age 51, was referred to us by a surgeon whom she had consulted because of a mass in the left axilla, about 10 cm. in diameter, which gave her pain and discomfort. Upon examining the breast, a smaller mass, about 4 cm. in diameter, was found close to the nipple in the upper and outer quadrant.

Radiation therapy was started Aug. 20, 1941, and was carried through daily, except Sundays, until Sept. 22. The breast and axilla each received 3,000 r, as estimated at tumor depth, and approximately 9,500 r measured at the skin with back-scatter. Radiation factors were: 200 kv., 4 ports, each 12 cm. in diameter, distance 50 cm., 1.0 mm. Cu + 1.0 mm. Al filtration, 5 ma. each target, average treatment time 22 1/2 minutes.

Both masses have completely disappeared. There was a slight epithelitis because of unavoidable overlapping. Over five years have passed and there are no signs of recurrence, nor are there any lung changes.

**CASE IV:** Mrs. D. L., white, age 33, married, with two children, gave a history of a lump in the left breast in 1938, for which mastectomy was performed. The pathological findings are not known.

In 1940, a mass appeared in the right breast, with small palpable nodes in the right axilla; several small nodules were found in the scar of the left breast, which had been amputated eighteen months before. Biopsy revealed metastatic adenocarcinoma in the nodules in the scar tissue and in the mass from the right breast.

Radiation therapy was begun Dec. 18, 1940, and carried through until Dec. 31. Each breast received 2,000 r at tumor depth, and the same dose was given in the axilla and supraclavicular regions. A second series was begun on May 21, 1941, and carried through to June 4. The dose was the same as in the first series. Between the two treatment periods, *i.e.*, Jan. 23 to Feb. 2, a sterilizing dose of radiation was administered to both ovarian regions. Each ovary received 1,850 r, as measured at depth, or 4,560 r as measured on the skin.

Five years have passed, and the patient is in excellent health, with no signs of recurrence or any pneumonic changes.

**CASE V:** Mrs. D. C., white, age 55, was sent to the hospital Aug. 5, 1942, with hemorrhage from the cervical stump and a history of loss of weight and strength. The body of the uterus had been removed three months earlier. On inspection, the cervix was found to be fixed, very vascular, and rough and granular in appearance. A biopsy was done, and a diagnosis of cancer, grade 3, was made. Radiation therapy was advised.

Multiple-port cross-radiation was started on



Fig. 10. Case VII: Involvement of the rectum secondary to carcinoma of the cervix. Views made on March 28 (A) and May 15 (B), before and after roentgen therapy, respectively.

Aug 10, 1942, and was carried out daily, except Sundays, with a rest period between Oct. 31 and Nov. 8 and another between Nov. 19 and Dec. 12. Forty-two treatments were given, averaging 180 r at tumor depth, totalling 7,615 r. The skin dosage was distributed over 40 fields, *i.e.*, 8 anteroposterior, 8 postero-anterior, 8 right lateral, 8 left lateral, and 8 perineal. The total skin dose measured in air, with back-scatter, was 44,480 r.

The skin reaction was very slight. There was some disturbing reaction in the colon and the urinary bladder, which necessitated the rest periods mentioned above. The patient made an uneventful recovery and is in apparent good health at the present time. Photographs of the cervix, taken before and after treatment (see color plate), show remarkable results.

**CASE VI:** Mrs. O. B., white, age 49, was admitted to the hospital Feb. 23, 1943, because of severe uterine hemorrhage of about one month's duration. On examination, we found the body of the uterus about the size of a large grapefruit. Through the cervical os protruded a large mass which was partly necrotic and very vascular. The biopsy report was grade 4 carcinoma. The case being considered hopeless, x-ray irradiation was recommended for control of bleeding. Meantime, supportive treatment was given in the form of blood transfusions, medication, and good nursing care.

Simultaneous cross-radiation was commenced on Feb. 23, 1943, and continued daily, except Sundays, until March 31. During that period, the patient received 6,814 r at center of tumor, with a skin dose of 50,816 r distributed through 40 separate ports. On examination at the end of treatment, it was surprising to see smoothing and regression of the tumor which had been protruding through the cervical os. The cervix was inflamed.

At this time the patient had regained some strength and weight and had begun to feel better. On May 25 she was brought back to the hospital because of recurrent hemorrhage. A second series of cross-radiation was started and continued daily until June 4. Eight treatments were administered, totalling 2,200 r at tumor depth or 8,800 r distributed through 40 ports over the skin.

Death occurred suddenly on June 5, from a coronary thrombosis.

**CASE VII:** Mrs. M. L., white, age 54, had passed through the menopause six years previously. One year before admission bleeding had begun and was treated by intra-uterine radium application for 48 hours (dose unknown). Hemorrhage ceased for six weeks and then recurred. Hysterectomy was suggested but refused, and the patient was referred for palliative radiation treatment.

Examination revealed total erosion of the cervix, and extension of growth to the posterior vaginal



wall, and involvement of the rectum. The patient required daily purgation and enemas. She refused a colostomy, which seemed inevitable. Treatment was administered daily from March 28 to May 1, 1944, except Sundays, averaging 150 r to the tumor. Measured *in vivo*, the dose totalled 3,000 r to the center of tumor, filtered through 1.75 mm. Cu + 1.0 mm. Al. There was a slight bronzing of skin at the end of the treatments, as well as slight nausea, which was easily controlled.

Because of the extensive involvement, small daily doses of spray radiation were given to the entire abdomen with the hope of producing an inversive reaction in the lymphatics. Following treatment, there was no further clinical manifestation of neoplastic involvement of the abdominal structures. This empirical procedure was based upon observation of a number of cases where palliative treatment had been given to bone metastases from a carcinoma of the breast, and where involution of axillary nodes had been noted, even though the breast and axilla were out of the range of the x-ray beams.

A roentgenogram prior to treatment showed a narrowing of the rectum. Six weeks later, the filling defect had disappeared, as had the mass in the vaginal wall. The bowels moved normally and the cervix became rounded and took on a normal appearance.

The patient lived in fair comfort for about one year and died from a metastatic lesion of the brain.

**CASE VIII:** C. D., male aged 40, was referred on March 1, 1941, because of a swelling at the angle of the right mandible. The mass had been developing for about one year, but had enlarged rapidly the month preceding admission. The patient had difficulty in opening his mouth because of the pain and swelling and had been subsisting on liquids, chiefly milk, for about three weeks. The tumor was hard and firm, and a diagnosis of carcinoma of the parotid gland was made.

Radiation with the multiple port tube was started on March 1, 1941, and carried through until April 9. A second shorter series of treatments, beginning May 5 and continuing daily to and including May 12, 1941, was also administered. The daily dosage was 150 r to the center of the tumor through 4 ports, with 2.0 mm. Cu + 1.0 mm. Al filter, 200 kv., 5 ma. The total dose was 3,600 r.

The tumor receded long before the completion of the first series and, after the second series, completely disappeared. At the present time, five years later, the patient is well and shows no sign of recurrence.

**CASE IX:** Mr. A. G., age 72, came to the hospital on July 29, 1941, with a diagnosis of inoperable carcinoma of the prostate gland. He wore a retention catheter and a portable urinal strapped to his thigh. The gland was large and nodular.

Palliative x-ray therapy was started on the day

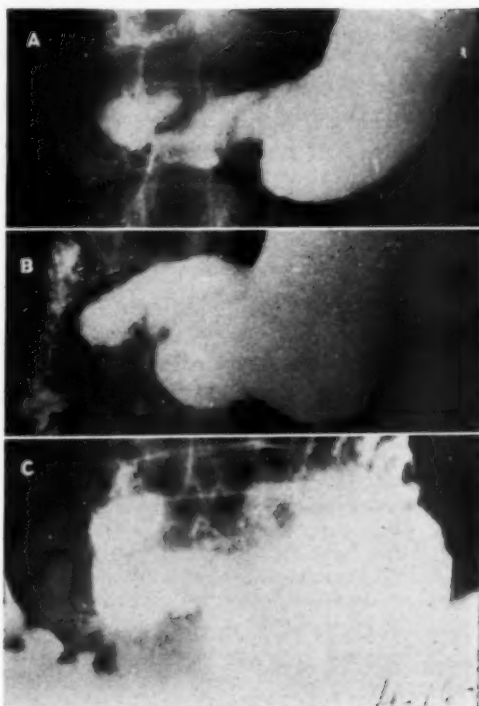


Fig. 11. Case X: Carcinoma of the stomach. Successive views, Oct. 18, 1940 (A), Feb. 4, 1941 (B), and April 16, 1941 (C).

of admission and was administered for eighteen days, omitting Sundays. The dose was 200 r daily, measured at depth. The superficial skin dose was 165 r at each port, totalling 660 r per treatment. The total depth dosage in the first series was 3,600 r calculated at tumor depth; total skin dosage 12,000 r including back-scatter. By mid-September the prostate was greatly diminished in size and the patient was advised to discard the retention catheter. It was found that he had control of the sphincter and was able to void voluntarily.

A second series of treatments was given between Sept. 29 and Oct. 6, inclusive, totalling 1,000 r at tumor depth, or 5,280 r distributed over the skin. The ports of entry numbered 40—8 anteroposterior, 8 right lateral, 8 postero-anterior, 8 left lateral, and 8 perineal.

The patient lived in comfort until February 1943, when he died of pneumonia.

**CASE X:** E. L., white male, age 62, had stomach trouble for a number of years. He had recently vomited blood and coffee-ground material, had lost 14 pounds in four weeks, and was dehydrated. X-ray examination showed a large filling defect in the prepyloric region. The diagnosis was probable cancer of the stomach. The attending surgeon suggested gas-

tric resection, but the patient refused. He was referred for radiation therapy, and two series of treatments were administered.

The first course began Nov. 15, 1940, and extended to Dec. 9, 3,000 r being given to the center of the tumor through 1.75 mm. Cu + 1.0 mm. Al. A second series of 2,700 r was administered from Feb. 4 to Feb. 23, 1941, with the same factors. No untoward effect was noted, beyond a slight bronzing of the skin. The lesion diminished gradually in size, and the patient regained his lost weight. In April 1941, on recheck roentgenography, a very small filling defect was still present, and a third series of irradiation was recommended.

The attending physician objected to further x-ray treatments on the assumption of a possible erroneous diagnosis for, as he put it, he had never heard of anyone being cured by radiation and the patient felt quite well at that time. One year later the patient was operated upon for an obstructive lesion and was found to have large metastatic masses in the liver and omentum, which confirmed the original diagnosis.

It is not certain what further radiation treatments might have accomplished in this case, but for a brief period, at least, palliative relief was obtained.

**CASE XI:** D. A., a 3-year-old boy, was brought to the hospital Oct. 29, 1940, with a swelling in the right sacroiliac region. Thirty days earlier he had complained of pain in the back, but as there was no swelling or tenderness at that time, the mother attributed his complaints to a sprain. Two weeks later, she discovered a tender mass over the right sacroiliac region. An x-ray film at that time showed an osteolytic tumor which, on aspiration biopsy, was diagnosed as sarcoma.

Simultaneous cross-radiation was started on the day of admission and continued through Nov. 8, by which time the tumor had disappeared entirely. The average daily dose was 150 r estimated at tumor depth, through 1.0 mm. Cu + 1.0 mm. Al, with 4 simultaneous ports, 200 kv., 5 mm., average time 11 minutes.

A second series of simultaneous cross-radiation was administered from Nov. 23 to Nov. 28, inclusive, with the same factors as above. The total dosage at the center of the tumor was 2,146 r.

Now, six years later, the child appears to be perfectly well and shows no sign of recurrence.

Reviewing the whole series of cases treated from August 1939 to August 1946 by simultaneous cross-radiation, we find that results vary in diminishing effectiveness. In the list below, the most gratifying results are given first.

1. Lymphogenous group, including Hodgkin's disease, leukosarcoma, etc.
2. Adenomas, both benign and malignant, particularly prostatic, salivary gland, and thyroid tumors.
3. Mammary gland neoplasms.
4. Uterine tumors, especially adenocarcinomas; to a lesser degree, the squamous type.
5. Tumors of the bladder.
6. Gastric and intestinal cancer (gratifying palliation).
7. Bone tumors of metastatic origin. (A single case of osteogenic sarcoma was treated successfully as reported above.)

#### CONCLUSION

A method of treatment has been described whereby one can administer at depth radiation doses comparing favorably with surface therapy. Lethal doses can be given to malignant tissue with a minimal amount of radiation to normal tissues in the tumor bed. The rate of recovery being more rapid in the latter than in the intensely irradiated tumor cells, fibrils of new connective tissue, blood vessels, and other repair processes are projected from the tumor bed into the tumor proper, replacing the destroyed neoplastic tissue.

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#### REFERENCE

- LOEBELL, M. A.: Simultaneous Cross-Radiation. *Am. J. Roentgenol.* 39: 274-277, February 1938.

# Erosive Bone Lesions and Soft-Tissue Ossifications Associated with Spinal Cord Injuries (Paraplegia)<sup>1</sup>

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DURING THE PAST war large numbers of patients with spinal cord injuries were seen on the neurosurgical services of the specialized general hospitals in the zone of the interior. These injuries were due to direct wounds from high explosive fragments or bullets, or to crushing injuries of the spine associated with violent trauma. With modern methods of therapy, the life span of these paralyzed individuals has been greatly lengthened. In the course of their treatment many complications developed. The commonest of these were malnutrition, decubitus sores, urinary tract calculi, and spastic deformities. The bony prominences adjacent to the decubiti frequently became eroded. In addition, ossifications developed in the neighboring soft tissues. These ossifications and erosions have been of particular interest to us.

Following the First World War, Dejerine, Ceillier, and Dejerine (1, 2) observed the presence of ossifications in the soft tissues, chiefly around the joint capsules and femoral shafts, in 49 per cent of paraplegic patients and described them under the name of "*para-osteo-arthropathies*." They called attention to the lack of development of disintegrative changes of the joint surfaces which commonly occur in the tabetic arthropathies and also pointed out that pathological fractures were very unusual. Erosions of bone adjacent to sores were noted but no descriptions were given. Voss (3) completely reviewed the literature in 1937 and called attention to the development of these ossifications in a variety of diseases of the brain, spinal

cord, and peripheral nerves. He presented the following list of conditions in which soft-tissue ossifications had been observed:

## *Brain Diseases and Cerebral Hemiplegia*

- Epidemic encephalitis
- Progressive paralysis
- Syphilis of central nervous system
- Arteriosclerotic bleeding and thrombosis
- Embolic encephalitis
- Post-traumatic brain lesions
- Brain hemorrhage with intracranial hemangioma
- Cerebral hemiplegia of unknown etiology

## *Diseases of the Spinal Cord*

- Meningocele
- Traumatic section of cord
- Extramedullary tumor
- Myeloencephalitis
- Syphilitic meningomyelitis
- Tuberculous meningomyelitis
- Acute anterior poliomyelitis
- Funicular myelosis with circumscribed thrombosis
- Tabes dorsalis
- Syringomyelia

## *Diseases of the Cauda Equina*

- Compression of the cauda equina

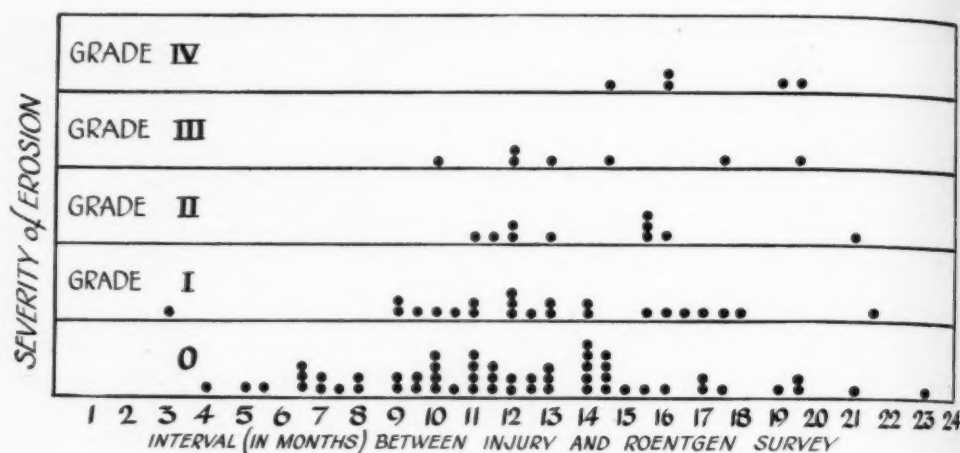
## *Diseases of the Peripheral Nerves*

- Polyneuritis

Recently Soule (4) has described the findings in a group of 62 patients with disease of the spinal cord and cauda equina under the title "*Neurogenic Ossifying Fibromyopathies*."

Roentgenologists assigned to the large general hospitals caring for patients with spinal cord injuries had the opportunity of observing the soft-tissue ossifications and the erosive bone lesions. It seems timely, therefore, to present a description

<sup>1</sup> Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.



Erosive changes in paraplegia: frequency chart.

of the roentgen findings since the detection of these lesions is primarily roentgenologic. It should be emphasized that the soft-tissue ossifications are not specific for spinal cord injuries but may develop in a great variety of diseases affecting the nervous system.

One hundred and nine cases of paraplegia were originally studied roentgenographically. Ten patients, however, upon completion of the survey, had been transferred to other hospitals and their films and records were not available for final compilation, so that the present report is actually based upon 99 cases. These have been arbitrarily divided into four groups depending upon the severity of the erosive bone change (Table I). The length of time

development of any single bone lesion or soft-tissue ossification is not known for any case of this series.

The roentgen survey included stereoscopic films in the anteroposterior projection of the lower lumbar spine, pelvis, and hips in all cases. Additional views of the knees, ankles, and heels were obtained in about 25 per cent of the group.

Of the 99 patients, 45 showed erosive bone changes aside from osteoporosis. Forty-three patients revealed soft-tissue ossification either contiguous with or apart from the skeleton. In only 4 cases with soft-tissue ossifications were there no associated bone changes. It is likely that if the study had been more complete, *i.e.*, if every part of the body below the level of the cord lesion had been studied, the incidence of soft-tissue ossifications would have been higher. In this series the percentage lies between that reported by Dejerine, Ceillier, and Dejerine, 49 per cent, and that reported by Soule, 33 per cent.

All of the previous reports of soft-tissue ossifications associated with lesions of the central nervous system stress the absence of accompanying bone lesions aside from the osteoporosis of the involved parts which invariably follows the disuse. In conducting our survey, we were impressed by the erosions of the trochanters which

TABLE I: CLASSIFICATION OF CASES ON BASIS OF EROSIIVE BONE CHANGES

Erosion	Erosive Bone Lesion	Soft Tissue Ossification	Total Cases
0	0	4	54
Grade I	23	17	23
Grade II	10	10	10
Grade III	7	7	7
Grade IV	5	5	5
	45	43	99

from the date of injury to the date of the survey is well illustrated in the accompanying frequency chart. The average was twelve months or more. The earliest de-





Fig. 1. Well defined round ossifications in the perineum and at the top of the left trochanter, which developed within four months. Both trochanters show moderate (Grade II) erosive changes. This film was made on Jan. 31, 1946. No definite bone or soft-tissue changes had been demonstrable on Sept. 20, 1945.

The patient was injured by a bullet on April 6, 1945, and had a complete paralysis below D-10. Trochanteric and sacral sores developed about two months after the injury. The former tended to progress in size, while the sacral sore showed signs of healing after six months. In November 1945, an unsuccessful attempt was made to repair the trochanteric sores. The patient had mild flexor spasm of the lower extremities. From December 1945, he became progressively more ambulatory in a wheel chair and braces. His general health became better and the sores improved but did not heal completely.

were very striking in some cases. In addition, a few patients had erosions of the ischial tuberosities. The extent of the erosive change in most cases was directly related to the severity, size, and duration of the decubitus sores. Eighty-five per cent of this series had sores over the sacrum, the trochanters, or the ischial tuberosities.

We shall first review the soft-tissue ossifications as they have been described previously and as they have been observed in our patients, and then present the erosive lesions with a description of the pathological findings.

Since the greatest number of roentgen studies in this series were made on an average of at least twelve months after the injury to the spinal cord, the ossifications were well developed and we did not

see any early lesions. In all probability, the precursor of the ossification is the laying down of flocculent, nebulous, or streaky amorphous calcium. Brailsford (5) has reported the presence of amorphous, flocculent calcification around the elbow in a case of hematomyelia of the cervical cord two months after injury. In another case of his in which there was known injury to the elbow joint, immediate radiographic examination revealed no changes; yet twenty days later there were woolly calcium deposits about the joint, and five weeks later well defined ectopic bone. As full development occurs, the bone may have compact or spongy components, or both, and may be in the form of small irregular fragments, in spicules, or in large irregular masses (Fig. 1).

Ossifications are most often seen in the



Fig. 2. Well defined ossifications below the femoral necks and at the superior acetabular lips. There are faint ossifications at the tops of the trochanters and early (Grade I) erosive changes of the trochanters.

This soldier sustained a fracture of C-5 on Aug. 17, 1944, following a driving accident. He had a complete paralysis with the level at C-6 and C-7. Sacral and trochanteric sores developed about four weeks after injury. The sacral sores healed in about three months, but those over the trochanters were still present in January 1946. The patient's general health has always been good and he has been very active in a wheel chair. Due to the limitation of use of his upper extremities he has never been up in braces. There is moderately severe flexor spasm of the legs. [Legend for Fig. 3 on opposite page]



Fig. 4. Large bony mass extending downward and posteriorly from the ischial tuberosity.

This patient was injured on Nov. 11, 1944, sustaining a complete paralysis with the level at D-11. His general condition has always been good and no decubitus sores have ever developed. The large mass of mature cancellous bone was noted during the survey and had not been suspected clinically.

vicinity of the larger joints, especially the hip and the knee. They may occur in muscles, tendons and sheaths, in ligaments, in the joint capsules, or be attached to the periosteum. In the region of the hip they are commonly seen in the lower part of the capsule or they may be extracapsular (Fig. 2). In many cases they seem to arise from the acetabular lips. They are commonly seen at the tops of the trochanters, seemingly contiguous to the trochanteric bone, and are most likely formed at the sites of the muscle attachments. About the knee they are most frequently found along the medial side in the region of the medial collateral ligament, but as a rule they are somewhat more extensive than is usual in Pellegrini-Stieda's disease. In

some cases they may occur in the fascial planes or deep muscles of the thigh, usually on the medial side or in the buttocks (Fig. 3). When in the fascial planes they are arranged in spicules; in the muscle they may present themselves as large masses of mature cancellous bone (Fig. 4). When the ossification is massive, it may completely ensheath a large joint and make it immobile.

The French authors (1, 2) who have the largest series have stressed the fact that the periosteum adjacent to the ossifications shows no changes. Even though the new bone formation is extensive and contiguous to the periosteum, it does not affect the periosteum or arise from it. It may be lightly attached to it in one or two areas.

The ossifications usually form within a

Fig. 3. Streaky ossifications in the deep fascial planes of the thigh medial to the lesser trochanters and at the tops of the greater trochanters. The greater trochanters show bilateral erosive changes (Grade II).

This patient was injured on January 1, 1945, by a shell fragment which completely severed the cauda equina at L-1. Two months later bilateral trochanteric sores appeared and they gradually increased in size. The general nutrition was poor and there was severe pain. In July 1945, a cordotomy was done for relief of pain. This lasted for three months and there was some general improvement. The pain then recurred, and the general condition regressed. The decubiti have persisted. The patient has never been ambulatory.

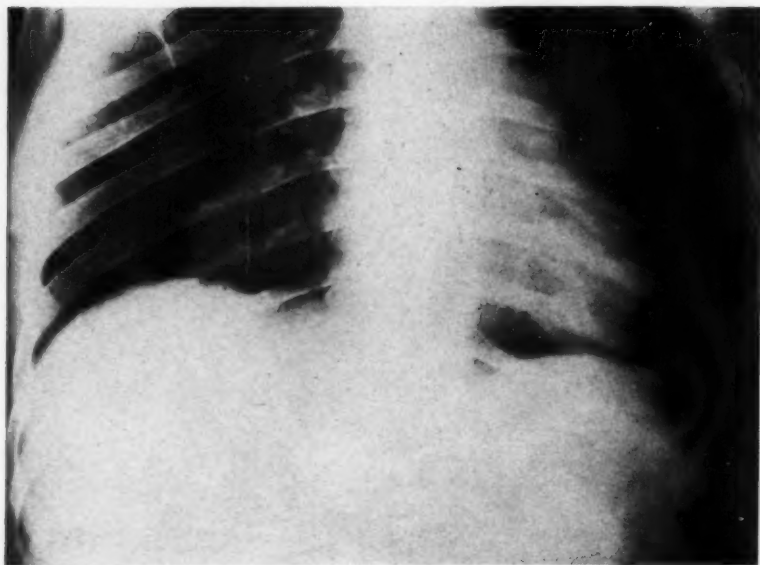


Fig. 5. Complete paraplegia with the level at C-7. Note the well developed ossifications of the intercostal muscles.

few weeks or months of the onset of the spinal cord injury. In only one case was late development observed, and this occurred two years after the injury. After they have assumed a mature trabecular pattern, the ossifications tend to remain constant in appearance, without increase in size or density. Additional centers do not develop adjacent to the older ones. This is the rule in the paraplegics where the nerve lesion is constant and non-progressive. However, in progressive diseases like tabes or syringomyelia, new centers of ossification may appear. On the other hand, in myositis ossificans due to direct trauma the ossifications, when fully developed, tend to regress. This regression is not observed in those ossifications which form under the influence of neurogenic disorders.

The ossifications are usually parallel or oblique to the shafts when they are in the muscles and should not be confused with the new bone formation of sarcoma, which, as a rule, is perpendicular to the shaft. They usually extend in the direction of the muscle fibers in which they are located (6) (Fig. 5).

Those soft-tissue ossifications which form following lesions of the spinal cord are never seen above the level of the lesion.

The erosive bone changes may be early or late. The earliest erosive change to be noted is a loss of the cortex of the greater trochanter without any reactive change of the underlying bone. Although the cortex in this area is normally thin, it is usually sharply defined in the roentgenogram. With the loss of cortex, the bone surface becomes roughened and slightly shaggy in appearance. Twenty-three of our cases showed this early change and 17 of these had associated ossifications in the soft tissues. Most of these were adjacent to the tops of the trochanters and extended above them for a few millimeters (Fig. 6).

As the loss of bone becomes greater and the lesions increase in severity, the trochanter loses its normal outward bulge and seems to extend upward in a straight or curved line, flush with the cortex of the femoral shaft directly below. This flattened appearance is due to complete loss of the trochanteric bulge (Fig. 7).

In the more advanced cases, in addition



Fig. 6. Ossifications below the acetabula on both sides. The one on the right is continuous with the superior lip of the acetabulum. There are Grade II erosions of both trochanters.

This patient was injured on Feb. 4, 1945, by a bullet, which produced a complete paralysis with the level at D-8. Decubitus sores developed over both trochanters nine months after injury. They became progressively worse, with a fair degree of surface infection. The sores were closed surgically after they had been present for six months. The patient's general condition has always been poor.

to the erosion and flattening, the impression is gained that there is a reshaping or moulding of the upper femoral shaft in the region of the erosive process. The bone, instead of being just flattened, has a curvilinear contour with pointing of the superior portion of the uneroded trochanter. The pointed portion is at the site of muscle attachments, and muscle pull probably plays a role in its formation. Usually there are, in addition, ossifications in the soft tissues above the pointed top of the trochanter and between it and the ilium (Fig. 8).

Evidence of healing of the erosive process is noted when the outer contour of the bone becomes more sharply outlined. Where the healing is more extensive, there may be bony proliferation, either shaggy or smooth. The outer curve of the trochanter may be restored to some degree as a smooth excrescence or it may be quite

shaggy, similar to the irregular repair seen in some fractures or in cases of arrested osteomyelitis (Fig. 9). It may be that as the healing stage is followed for greater lengths of time more cases will show evidence of proliferative repair of the surface.

Some cases have shown other changes which might be considered as complications. One patient with very severe erosive changes of the trochanters and ossifications in the soft tissues had a subcapital fracture of the neck of the left femur from severe flexor spasm. The type of fracture is similar to that described by Batt and Hampton (7) in tabes.

In another case there was a subluxation of the right hip joint which was associated with severe spasticity. An additional case showing severe erosive changes presented shaggy bony periosteal proliferations of the femoral shaft below the level of the erosions, of the type usually seen when





Fig. 7. Grade IV erosive changes of the trochanters. Note the moulding of the outer aspect of the left femoral shaft.

The patient was injured on July 6, 1944, with complete paralysis below D-4. The sacral sores healed in ten months but the trochanteric sores were still unhealed in January 1946. There has been a marked degree of flexor spasm and pain. A tractotomy was performed in December 1945, but this was unsuccessful and the spasm is still severe. The patient became fully ambulatory in a wheel chair in January 1946 and ambulatory in braces a month later. His general condition has improved but at the time of ambulation in braces the sores were still unhealed.

there is infection of the soft tissues adjacent to the bone. In this instance there was extensive purulent infection of the sores and the deeper tissues of the thighs (Fig. 10).

In summary, the distinctive skeletal features as they are noted in the roentgenograms are, first, erosive changes leading to loss of the normal contour of the trochanters with flattening, followed by reshaping or moulding, and later repair of the eroded surface with formation of an abnormal contour by proliferative or exuberant bone. Secondly, and just as striking as the bony change, is the complete lack of any joint surface involvement or diminution of the joint space. All cases show osteoporosis of varying degrees.

There was no autopsy material available for study. In order to evaluate the exact nature of the erosive process, biop-

sies of trochanteric bone were obtained from 10 patients who were to have secondary closures. By cutting through the granulation tissue into the underlying bone, wedges of bone were obtained with an osteotome. These went to a depth of 1.0 to 1.5 cm. In one case, a small fragment of bone lying loose in the granulation tissue was studied.

Sections were made and these were reviewed by Dr. Henry L. Jaffe (8), whose description is as follows:

"All of the tissue slides show extensive subacute and chronic infection of the soft tissues overlying the bones and extension of the infection to at least the superficial portion of the bone. The involvement of the bone itself is manifested in several ways and to several degrees. The mildest degree of involvement is registered in increased vascularization of the more super-



Fig. 8. Extensive (Grade IV) erosive changes of both trochanters. Note the complete loss of the left trochanteric bulge and the appearance of moulding of the outer surface. There are extensive soft-tissue ossifications at the tops of the trochanters on both sides and at the top of the right iliac crest. Note those below the right lesser trochanter.

This patient was injured on Oct. 7, 1944, by a shell fragment which caused a complete lesion at D-6. Sores over the sacrum and trochanters developed one month later. Two months after injury skin grafts were attempted on the trochanteric sores but they were unsuccessful. The patient was left on his back during this time and flexion contractures of the legs developed. The sacral decubitus increased in size. In July 1945, a pinch graft was attempted on the trochanteric sores but was only 25 per cent successful. The flexion contractures persisted, and a bilateral hamstring tenotomy was performed but was unsuccessful. This was later repeated and at that time it was found that the sciatic nerve and blood vessels of the lower extremities were bound up in scar tissue. They were mobilized. The patient has been up in a wheel chair since June 1945, but has never been ambulatory in braces. The sacral sore is now healed and the trochanteric sores are minimal in size.

ficially placed spongy marrow spaces, and some inflammatory resorption and atrophy of the osseous tissue. From this mild stage, there is a gradual step-up in various specimens to extensive low-grade inflammatory invasion of the marrow spaces characterized by fibrous and vascular tissue filling the marrow spaces, which have become enlarged. In this tissue, some inflammatory cells are seen, most of which are mononuclear cells. Concomitant with encroachment on the marrow spaces by this inflammatory fibrovascular tissue there are progressive atrophy and resorption of the osseous tissue proper. Finally, in some of the sections, one notes actual ac-

tive osteomyelitis with extensive necrotization of the osseous tissue and even what amounts to potential sequestrum formation." (Fig. 11.)

What is the sequence of events in these patients which allows the pathological change to develop? Marked weight loss with accompanying soft-part atrophy becomes evident soon after the spinal cord injury. The commonly complicating decubitus sore also forms within a short time. The weight loss, the atrophy of the soft parts, the development of the decubitus with a low-grade infection, the anorexia and digestive disturbances are all clinical evidences of a malnourished state. Their



Fig. 9. Good example of proliferative repair on the right following the healing of trochanteric sores by secondary closure.

This patient was injured on Aug. 20, 1944, with a complete paralysis below D-7. Sores over the sacrum and both trochanters developed three weeks after injury, increasing in severity until February 1945. They then remained static in spite of partial ambulation. An attempt at closure was made in July 1945 but was unsuccessful. Closure was accomplished in September 1945. The patient became completely ambulatory in braces in November 1945, and his general condition has improved markedly. Rather severe flexor spasm of the lower extremities is still present.

correction and the restoration of adequate nutrition constituted one of the most difficult problems in the general medical care of these patients. It was observed that when the nutrition was improved the sores healed more easily or, if secondary closures were necessary, they were more successful (9). It seems quite probable that without the active medical and nursing care given to these patients in order to restore, maintain, or improve their nutrition, many would not have survived. Since they did survive, even in the presence of the severe sores with low-grade infections, the extensive erosive bone lesions which had not before been observed roentgenographically have developed.

It may be stated categorically that the most striking lesions have occurred in the patients whose decubitus sores persisted for the longest periods of time. With the

development of the sore, the marked soft-part atrophy over the trochanter, and the routine in which the patient is turned from side to side, so that he is lying first on one trochanter and then on the other, direct pressure is exerted on the outer aspect of the trochanteric bone. The periosteum is soon affected by this pressure and devitalized, exposing the cortex to the low-grade surface infection. The presence of the sore and the infection produces a local hyperemia. Following treatment, the sore may become relatively clean, with a granulating surface, but the hyperemia persists. The hyperemia and the infectious process lead to absorption of the surface trabeculae, which becomes greater and more extensive as long as the sore remains unhealed. The extent of the erosion and the extent of the fibrovascular reactive change in the bone marrow are dependent



Fig. 10. In addition to the erosions this case illustrates the usual type of shaggy periosteal proliferation secondary to infection. This was the only case in the series with this type of periosteal proliferation.

The patient was injured in November 1944, by a shell fragment, which caused an incomplete lesion of the cauda equina. He was in good condition when he entered the hospital but decubitus sores appeared five months after his injury. In February 1945, his nutritional state began to decline in spite of all therapeutic procedures, as repeated transfusions, intravenous amino acids, amigen, concentrated albumin, and plasma. The sores on the hips became worse. The patient has never been ambulatory in a wheel chair or braces. Dependent edema and ascites were noted when the hypoproteinemia was severe. The sores and surrounding tissues of the hips and thighs were heavily infected and purulent at all times. There was moderate adductor spasm.

upon the degree of hyperemia and infection.

In this series of cases there were no joint lesions suggestive of the neuro-arthropathies. Although arthropathies do develop in non-weight-bearing joints such as are seen in the elbow and shoulder in tabes and syringomyelia, it must be emphasized that the joints in paraplegia are not subjected to repeated trauma, as there is loss of motor control as well as sensation. In addition, in the recumbent position the joints of the lower limbs are non-weight-bearing. However, in the general treatment of these patients one of the ultimate goals was to make them ambulatory in braces. This was attempted as soon as their clinical condition permitted. An additional survey

was made of 50 patients who were ambulatory for various periods up to six months, most of them for at least four months. No disintegrative lesions suggestive of an arthropathy were observed.

The only arthropathic change that has been observed is in the one case with a subcapital fracture due to severe flexor spasm. Here the femoral head is intact, but there are loose bony fragments lying free in the capsule, and the appearance is similar to that of a neuro-arthropathy (Fig. 12).

It is interesting to speculate whether arthropathies will develop in the ambulatory patients. It may be that, as they become more and more ambulatory, changes will be seen, since factors such as weight-

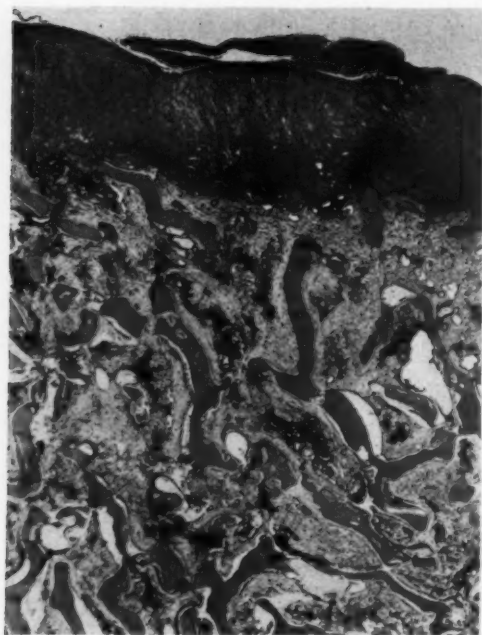


Fig. 11. Low-power photomicrograph of biopsy specimen showing the characteristic pathological changes. Note the granulation tissue overlying trabeculae in various stages of resorption. The cortex is completely gone. The fatty marrow has been replaced by fibrovascular tissue.

bearing and anesthesia which favor the development of an arthropathy are present. With ambulation the joints will be exposed more frequently to trauma, even though the limbs are protected by braces. It will also be interesting to observe whether there will be any atrophy of bone such as occurs in the metatarsal heads in anesthetic leprosy. Here there is no infection, but the heads and shafts are subjected to direct pressure in the absence of sensation. They disappear while the phalanges remain (10). Further follow-up on these patients at stated intervals would seem to be indicated.

The nature of the underlying cause for the development of the soft-tissue ossifications is not clear nor is it fully understood. The question of trauma to the soft tissue has been noted by previous writers, and there is some evidence to support this contention. As mentioned above, calcification in the soft tissue around the elbow

developed in twenty days after known trauma in one of Brailsford's cases. Delano (11) has recently discussed the relationship of the trophic control of nerves to bone and joints as against trauma as a cause of the arthropathies. He feels that the majority of evidence favors trauma and reports one case of extensive ossification about the right hip in a case of paraplegia. The paraplegia had been present for fifteen years and the patient was always turned on the right side, and never, or very rarely, on the left. This subjected the right hip to trauma and pressure.

Since these patients are completely dependent from the moment of injury, it is conceivable that trauma to the soft tissues may occur. They do not have normal sensation and must be moved frequently. Early in the disease they may have been handled roughly or treated clumsily. With this type of handling, the soft tissues may have become traumatized. Whether unrecognized hematomas have formed at the sites of injury in the soft parts and have acted as a basis for the deposit of calcium cannot be said, but this is a possibility.

On the other hand, the neurogenic influence in the development of the soft-tissue ossifications cannot be disregarded because of their high incidence in neurologic disorders. Even though the factor of trauma may be an important one, it may not be the only one. The development of traumatic myositis ossificans in the injured limbs of the thousands of war casualties in the absence of neurologic disorders was certainly infrequent, while soft-tissue ossifications without definite known trauma are quite frequent in the group of cases which we are discussing. As has been pointed out by Delano, the existence of true trophic nerves has not been proved; yet these patients do have evidence of disturbance of the autonomic nerve supply below the level of the lesion. It may be that trauma to the connective tissues acts as an accessory or trigger factor in the development of the ossifications when there is a disturbance in the nerve supply.





Fig. 12. Bony fragmentation at the site of a left subcapital fracture, suggesting an arthropathic joint; erosive changes of both trochanters, and soft-tissue ossifications adjacent to the tops of the trochanters.

This patient was struck in the back by a shell fragment on June 11, 1944. This produced a complete paralysis with the level at D-5. Within one and a half months bilateral trochanteric sores had developed. A sacral sore appeared a short time later and became healed only about 16 months after injury. The trochanteric sores were still unhealed in January 1946, but had shown gradual improvement and at that time were only minimal in size. Because of severe flexor spasm, the patient had been up in a wheel chair for only short periods of time and had never been ambulatory in braces. In December 1945, a subcapital fracture of the neck of the left femur was discovered during a survey for bladder stones.

With severe trauma there is a marked catabolic phase, as evidenced by prolonged negative nitrogen and calcium balances beginning shortly after the onset of injury (12). Although the values of serum calcium are not increased significantly, there is increased calcium excretion in the urine. The deposition of calcium in mesenchymatous tissues tends to occur when the normal metabolism is lowered (13). Does the loss of the normal nervous control to traumatized or normal connective tissue lower the normal metabolic level so that the mobilized calcium may be deposited?

As noted above, the earliest lesion observed is the deposit of amorphous calcium in the connective-tissue interstices of the muscles, ligaments, tendons, and joint capsules, or overlying the periosteum or

at the sites of the muscle attachments to the skeletal bones. As a rule, the ossification takes place directly in the calcified area of the connective tissue without the preformation of cartilage, although there is one case reported with precartilaginous formation (1).

Soule (14) believes that the early amorphous calcium deposit as observed in the roentgenograms of these cases is actually amorphous bone similar to callus. However, without histologic proof this cannot be positively assumed. Whether it remains as calcium in an amorphous state or develops into bone depends upon the presence of an adequate blood supply to the calcium mass.

In some cases there are rather extensive ossifications in the soft tissues adjacent to

areas of severe erosion. The inflammatory hyperemia must involve this whole general area, instead of being sharply limited to the area directly over the erosion. In the presence of hyperemia, decalcification usually occurs, and with a diminished blood supply calcium is laid down. What are the underlying factors which allow these ossifications to develop so close to an area of hyperemia? It is difficult to offer an adequate explanation for this paradox. Since there is evidence that the ossifications are present relatively early after the spinal cord injury, it may be that they are formed before the hyperemia of the area reaches its full development. After their formation the general hyperemia may not be extensive enough for their resorption.

#### SUMMARY

1. The erosive bone lesions and the soft-tissue ossifications which were observed in a survey of 99 cases of paraplegia have been described. Although they frequently occur in the same individuals, it is to be emphasized that etiologically they are unrelated.

2. The erosive lesions develop where soft tissue over bony prominences, as the trochanters, becomes devitalized. Pathologically this is evidenced by a subacute and chronic infection of the tissue overlying the bone, with extension to the superficial layers of bone. This leads to resorption of the cortex and underlying trabeculae. The bone marrow is replaced by fibrovascular tissue which accompanies the low-grade inflammatory process.

3. The factors relating to the formation of the soft-tissue ossifications have been considered. Although soft-tissue trauma may play an important role, the neurogenic influence cannot be disregarded.

NOTE: The authors are indebted to Dr. A. B. Soule, Jr., for his many valuable suggestions, to Dr. H. L. Jaffe for his kindness in examining the pathological material, to Dr. S. L. Meltzer for the use of some of his material, and to Capt. E. Ernst, Jr., for conducting part of the survey.

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#### DISCUSSION

Paul C. Swenson, M.D. (Philadelphia, Penna.): Dr. Heilbrun deserves a great deal of commendation for having made such an interesting and complete study of this unusual sequela in paraplegics. Apparently, more cases of this sort have been seen than during the First World War and they merit a rather complete analysis and study. The present description has been very complete and requires little comment or addition.

I would like, however, to discuss very briefly some of the points in the etiology. Just what should allow for this mobilization of calcium from the eroded bone and its redeposition in the soft tissues overlying it is a most intriguing question. For a number of years I have been interested in the bone thickening underlying the soft tissues where varicosities are found. Usually a diffuse condensation of the cortex develops, particularly when infection has supervened in the soft tissues containing the varices. In the poorly nourished tissues ulcers quickly develop, with subsequent infection, and I have seen a condition almost identical with what has been shown today

develop in just this situation. In order to have mobilization of calcium, one must have an intact blood supply. In the earlier stage of this condition, Dr. Heilbrun has shown that we have a hyperemia. This would account for the early mobilization of the calcium. Later, there is a decreased blood supply, which brings about a fibro-osseous reaction and is

responsible for the eventual bone production. Trauma, of course, plays an important role, as well as the lowering of the local metabolism.

As stated by Dr. Heilbrun, the neurogenic factor may be the primary one, followed by the others later. Further study is obviously required for an understanding of this particular situation.



## High-Intensity Radiation from

## Beryllium-Window X-Ray Tubes<sup>1</sup>

T. H. ROGERS

Springdale, Conn.

THE LOW ATOMIC number and low density of beryllium give it the lowest absorption coefficient of any material which might, by virtue of other suitable physical characteristics, be employed for windows in x-ray tubes. The first use of

but in an internal hood surrounding the target, the purpose of which was to prevent the bombardment of the tube walls by secondary electrons. Beryllium windows permit such hoods to shield completely against electrons while absorbing the x-ray

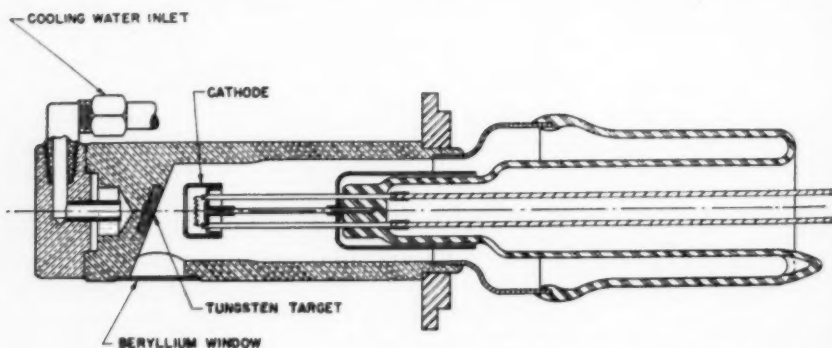
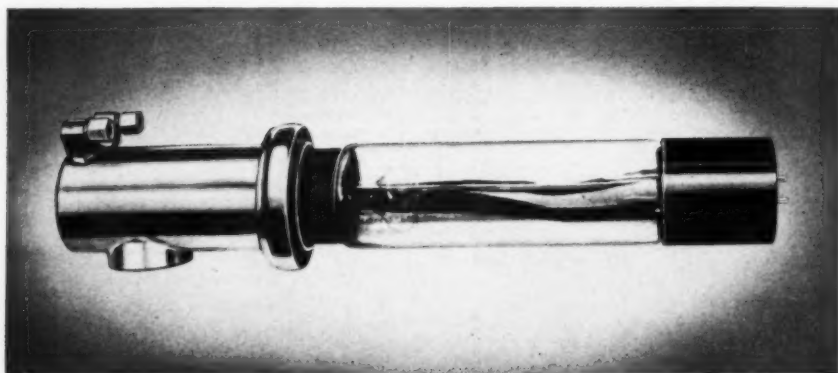


Fig. 1. Beryllium-window tube providing 40-degree x-ray beam. (Courtesy Machlett Laboratories, Inc.)

beryllium plates for such a purpose appears to have been in Germany, and shortly thereafter in this country, in the early 1930's, when they were used, not as windows in the external envelope of the tube,

beam to a negligible extent. There is, of course, no requirement that such windows be vacuum-tight, as is the case in the external envelope.

The development of malleable beryl-

<sup>1</sup> From the Engineering Department, Machlett Laboratories, Inc., Springdale, Conn. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

beryllium (1) and the production therefrom of thin vacuum-tight sheets led to the first commercially produced tubes with vacuum-tight beryllium windows in the external envelope, as reported by Machlett (2) in 1942. These tubes were designed primarily for x-ray diffraction work, having targets of special materials, such as molybdenum, cobalt, copper, iron, or chromium. The beryllium window was sought for such tubes in order to reduce to a minimum the loss of intensity due to absorption in the window of the characteristic radiation of the target material, which is of relatively

difficulties involved in the fabrication of vacuum-tight beryllium windows increase many-fold, particularly in the operation of brazing the windows in a permanently vacuum-tight manner to a suitable base for incorporation into the tube envelope. Nevertheless, the necessary technics have been perfected, and tubes with beryllium windows admitting a 40-degree solid angle cone of rays (Fig. 1) have now been available for some time (6).

As indicated above, such tubes were first developed to meet the needs of certain special radiographic applications, arising

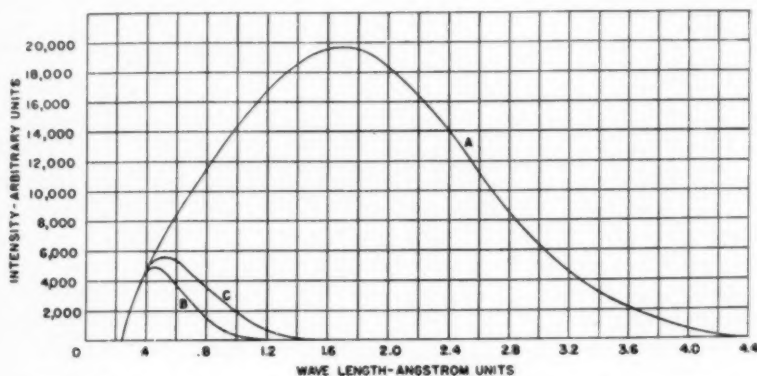


Fig. 2. Calculated intensity-wave-length distribution of x-radiation at 50 kv., (A) filtered by 1 mm. Beryllium; (B) filtered by 1 mm. Aluminum; (C) filtered by 1 mm. Pyrex glass. Intensity expressed in terms of ionizing power.

long wave length, particularly in the case of the lower atomic number materials like cobalt, iron, and chromium. In these and other tubes (3) designed primarily for diffraction studies, the window may be quite small, since only a narrow pencil of rays is employed.

The advantages of this low-absorption window for other applications were soon recognized, and these so-called "diffraction tubes" were used advantageously in such special radiographic procedures as micro-radiography (4, 5) and the checking of spot-welds of thin aluminum sheets. In some of these applications, a wider beam had to be employed to cover larger areas than was possible with the diffraction tubes, and a larger window was therefore required. As the size is increased, the

principally in connection with the war effort. It is natural to inquire whether they offer possibilities for advantageous use in the medical field, as well as in other industrial applications. To arrive at an answer to this inquiry, it is desirable to investigate the nature of the radiation obtainable from the tubes, both qualitatively and quantitatively.

The "quality" aspect of this radiation can probably be explored most readily by means of calculations based on Kramers' formula (7) for the energy of x-ray emission at all wave lengths throughout the continuous spectrum. The intensity-wave-length distributions for x-rays generated at 50 kv. and modified by absorption by a 1 mm. thickness of beryllium, aluminum, and Pyrex glass, respectively, have



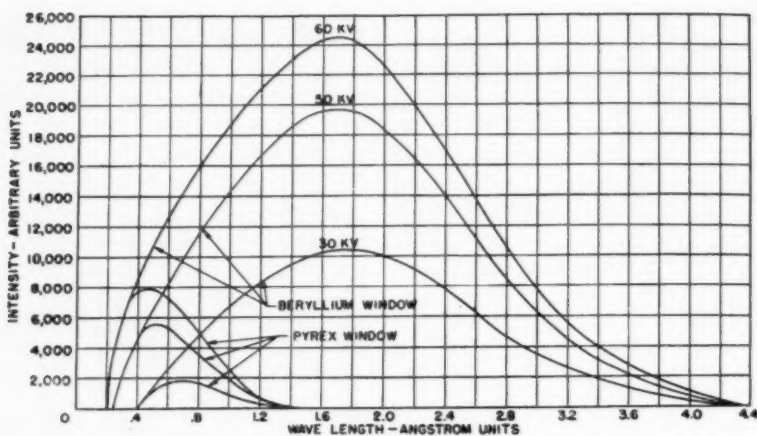


Fig. 3. Calculated intensity-wave-length distribution of x-radiation at 60, 50, and 30 kv. Window thickness 1 mm.

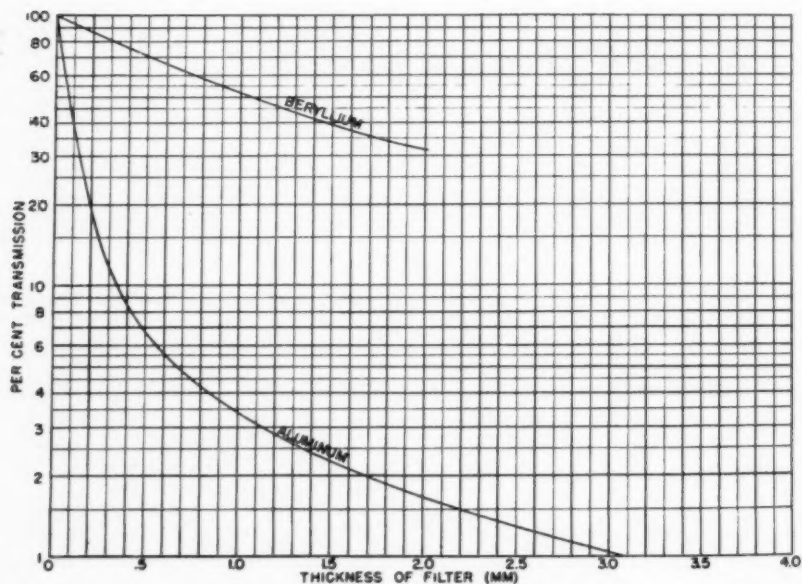


Fig. 4. Absorption curves for output of beryllium-window tube at 50 kv., with aluminum and beryllium filters, respectively.

been thus calculated (6), with results as plotted in Figure 2. The intensities are in terms of energy absorbed in air, expressed in arbitrary units, and are thus approximately proportional to roentgens per minute. These plots indicate, to some degree of approximation at least, the relative importance of each wave-length component

of the radiation making up the total intensity. It will be noted that a major proportion of the radiation obtainable from the beryllium-window tube consists of wave-length components which are entirely eliminated by a window of Pyrex or aluminum of equal thickness. An approximation of the relative total intensities

in the three cases may be obtained by integrating the areas under the three curves, giving proportions as follows: Beryllium, 100; Pyrex, 7.9; Aluminum, 4.9.

The relationship between voltage and wave-length distribution is indicated by a similar calculation for 60, 50, and 30 kv., respectively, with results as plotted in Figure 3. These curves show the relative outputs for a beryllium window 1 mm. thick and a Pyrex glass window 1 mm. thick at the three voltages. Integration of the areas under the respective curves indicates the following relative total intensities:

	60 kv.	50 kv.	30 kv.
Beryllium.....	100%	78%	40%
Pyrex.....	9.8%	6.2%	1.9%
Ratio $\frac{\text{Pyrex}}{\text{Beryllium}}$	9.8%	7.9%	4.8%

The physical measurement of the actual intensity in roentgens per minute of radiation containing wave-length components in the range admitted by the beryllium window presents certain difficulties not encountered in ordinary dosage measurements. The type of low-voltage chamber devised by Taylor and Stoneburner (8), used in the manner described by them for measurement of "Grenz rays," constitutes a suitable standard of accuracy in such dosimetry. Smaller chambers of the closed type, desirable for the sake of convenience in routine measurements, introduce considerable error unless adequate precautions are taken in their design and construction to avoid appreciable absorption in the wall.

Trout and Atlee (9, 10) made measure-

ments of the output of experimental beryllium-window tubes using the Victoreen thimble chamber. Their reports include only absorption curves showing percentages rather than absolute values. It is apparent that dosage values determined in this way will be in considerable error due to absorption in the chamber wall. The extent of the error is indicated by the subsequent work of Victoreen, Atlee, and Trout (11), which showed that at a wave length of 1.5 Ångströms, the Victoreen chamber gives a reading of only 50 per cent of the actual dosage. They describe an experimental chamber of beryllium, showing an error of 10 per cent at 1.5 Ångströms. Inasmuch as a major proportion of the radiation is at wave lengths greater than 1.5 Ångströms (see Fig. 2), even greater errors can be expected when measuring such radiation with chambers of these types.

The "mesh" chamber described by Quimby and Focht (12) for dosage measurements for "contact therapy" apparatus should give results of suitable accuracy with this radiation. Braestrup (13) has constructed a somewhat similar chamber employing extremely thin films of nylon coated with graphite, which is reported to give results comparable with the standard.

Measurements made by Braestrup (13) of the output of the large-beryllium-window tube described above, by means of the Taylor and Stoneburner chamber, provide a quantitative as well as qualitative indication of the intensity obtainable. The measurements are tabulated below, and the corresponding absorption curves are plotted in Figure 4.

kv. (c.p.)	T.D.	Added Filter	r/min./ma.	Percentage Trans.	h.v.l. in mm. Al
50	10 cm.	0	1,555	100	0.07
"	"	0.05 mm. Al	903	58	0.09
"	"	0.1 " "	605	39	0.11
"	"	0.5 " "	104	6.7	0.55
"	"	1.0 " "	53	3.4	0.94
"	"	2.0 " "	25.7	1.65	1.50
"	"	3.0 " "	16.1	1.03	1.71
"	"	5.0 " "	7.2	0.46	
"	"	0.5 " Be		71.0	
"	"	1.0 " "		52.0	
"	"	2.0 " "		32.5	
50	2 cm.	0	46,600		

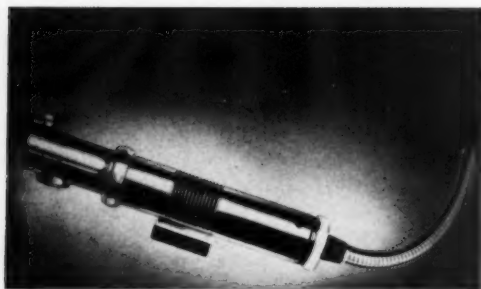


Fig. 5. Shock-proof tube with beryllium window; 40-degree x-ray beam. (Courtesy Machlett Laboratories, Inc.)

The value given for 2 cm. target distance is calculated from the measurement at 10 cm. by applying the inverse-square law and correcting for absorption in the intervening air on the basis of absorption per cm. at a 10 cm. distance. There is a certain amount of indeterminable error in both of these corrections, due to the focal spot being of finite size and due to the continuous change in quality with added air filtration, but the two elements of error are in opposite directions and tend to cancel each other.

Tubes of the type described are capable of operation at any voltage up to 50 kv., and with currents up to 50 ma. The properties of beryllium, in addition to affording minimum loss of radiation by absorption, permit locating the window very close to the focal spot, which would not be feasible with any other low-absorption material such as Lindeman glass, bubble type glass, or aluminum foil, because of the heating involved if high energies are to be used. Hence, a target distance of 2 cm. to the outer surface of the window becomes possible. On the basis of the output data of the above table, an intensity of 2,330,000 roentgens per minute is obtainable at this distance, with 50 ma. at 50 kv.

This high roentgen intensity, being so far in excess of values commonly encountered, suggests many intriguing possibilities. Numerous experiments have been performed on sterilization by x-rays. Those of Clark (14) and of Wyckoff (15)

agree with many others in showing a logarithmic death rate for bacteria subjected to large dosages. The dosages for complete sterilization have seemed, in the past, to be such as to preclude such processes on a commercial basis. The availability of dosage rates in the order of 2,000,000 r per minute can greatly facilitate such experiments and would render commercial utilization definitely feasible, at least for certain materials of high value. Examples of such applications are provided by recent experiments by Clark (16), which indicate definite success in the preparation of vaccines by the irradiation of bacterial suspensions, the bacteria being killed while the antibodies remain unaffected in the very short time required for the lethal dose with this type of tube. Other possibilities are the sterilization of suture material that cannot be subjected to sufficient heat to accomplish sterilization, and the sterilization of a wide variety of food products without subjecting them to flavor-destroying temperature.

Of more direct interest in the radiological field are the therapeutic possibilities of this new tool. While a dosage rate of 2,000,000 r per minute can hardly be used directly for treatment purposes, nevertheless an infinite number of possible combinations of voltage, milliamperage, distance, and filtration make available a wide range of dosage rates and depth dose factors, making such equipment adaptable for applications ranging from intracavity therapy to so-called "Grenz" ray therapy, including also the normal skin therapy applications.

For intracavity irradiation, which is usually done with so-called "contact" therapy apparatus, the compact shock-proof form of the tube, as illustrated in Figure 5, lends itself to the procedure of introducing into the cavity a field-defining tunnel or cone through which radiation from a distance of 10 cm., more or less, can be directed to the area to be treated, as indicated in Figure 6. The size of the cone employed need be no larger than the lesion to be treated. By proper selection of voltage, depth dose could be minimized

to any required degree, at least to the same extent as is accomplished with contact therapy, which depends on a very short target distance so that diminution in depth dose is partly dependent on the inverse-square law. Adequate studies of dosage rates and depth dose factors as a function of voltage, distance, and filtration will of course have to be made before such techniques can be established.

For therapy of most skin disorders, the work of Andrews and Braestrup (17) indicates a definite advantage in employing

a therapeutic medium. Beryllium-window tubes are ideally suited to the generation of such rays, without involving the fragility of previous Grenz ray tubes with their windows of Lindeman glass or very thin bubble-like glass. Inasmuch as operation may be at any desired voltage from 3 to 50 kv., possibilities of large scope exist for extending or improving on past technics in this field. Thus, in the therapeutic field, a single unit having sufficiently wide versatility to enable it to handle skin therapy, intracavity therapy, and Grenz ray therapy

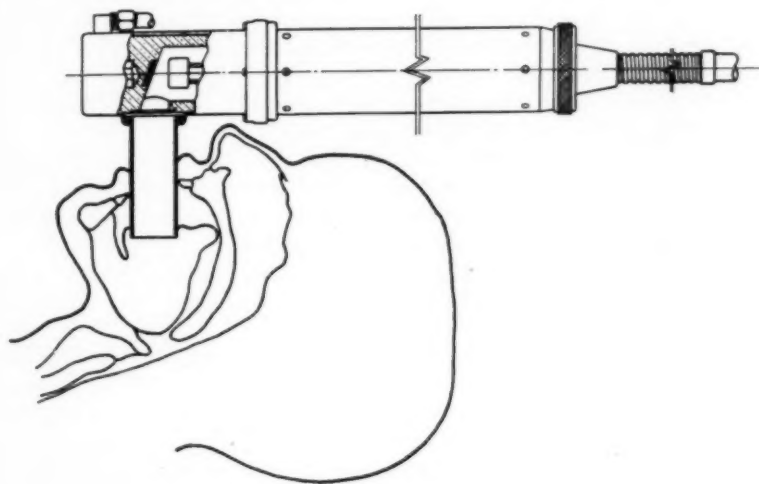


Fig. 6. Suggested arrangement for intracavity therapy.

kilovoltages considerably lower than earlier common practice, together with considerable filtration, so as to obtain quite homogeneous radiation of optimum penetration. Such technic requires a high milliamperage to obtain a reasonable dosage rate. The possibility is indicated that even lower voltages with higher milliamperage, such as are permissible with the presently available beryllium-window tubes, may result in optimum conditions for most such treatments. Thus another fruitful field for exploration is extended by these tubes.

The range of radiation designated as "Grenz" rays (18), usually considered to consist of radiation generated at from 3 to 12 kv., has found a degree of acceptance as

may be developed employing a tube of this type.

The potentialities of radiation of the nature obtainable from such tubes in the field of biological research, of direct and indirect interest to the medical profession, merit investigation by biophysicists and biochemists. The large dosage rates, easily controllable over a very wide range, present opportunities in that field too numerous to mention.

Outside of the medical and biological fields, opportunities for research and experiments in industrial fields are endless. X-ray photochemistry, wherein the nature of materials is altered by exposure to x-rays can be explored on a much wider basis than



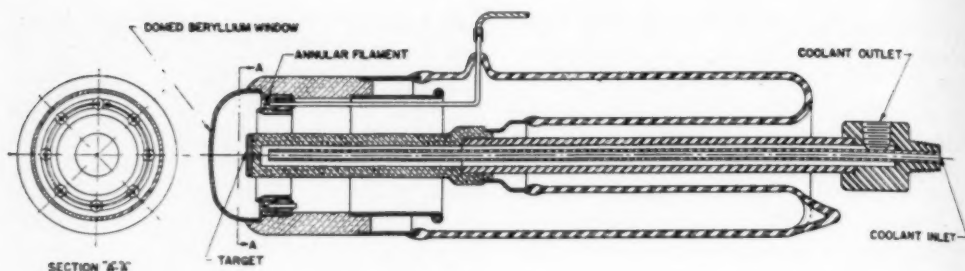


Fig. 7. Schematic view in section of beryllium-window tube providing 180-degree solid angle x-ray beam.

heretofore, now that a 2,000,000 r per minute source of rays is available. One example that naturally suggests itself is the possibility of assisting the research which is a necessary part of the atomic energy development program. Materials to be employed in atomic power plant engineering must be investigated as to their ability to withstand intense radiations of various sorts. Of the types of radiation involved, gamma rays are the most penetrating and probably present the greatest problem. Inasmuch as the effects of x-rays and gamma rays on material are similar, producing ionization which results in observable changes, the effect of very intense radiation on small samples of any desired material can be studied with extreme simplicity with such apparatus. A very interesting type of photochemical reaction, reported by Pough and Rogers (19), is the change in the color of certain gem stones when subjected to the radiation from these tubes for relatively short periods. Pale yellow sapphires have been turned to a brilliant orange by a five-minute exposure. Clear lavender specimens of spodumene have changed to a brilliant green, identical in appearance with the rare hiddenite variety. Another photochemical effect, of immediate interest to the medical profession, is the decomposition of sulfa drugs by x-rays. This reaction has been obtained and is being quantitatively studied by Clark (16), following clinical observations that patients who were given both sulfa drugs and x-ray therapy experienced no desirable effects from the former.

Clark (16) has also found that, with the

intense radiation obtainable with beryllium-window tubes, unknown materials can readily be analyzed as to chemical composition, both qualitatively and quantitatively, by spectroscopically analyzing the secondary characteristic fluorescent x-rays generated in a sample. With this primary source, the secondary rays are strong enough to be analyzed by a simple crystal spectrometer without any unusual arrangements.

To summarize, beryllium-window tubes now available provide a beam as wide as the usual diagnostic tube, namely, 40-degree solid angle cone, with the outer surface of the window approximately 2 cm. from the focal spot. Operating at maximum capacity of 50 ma. at 50 kv., such tubes make available a dosage rate in the order of 2,000,000 roentgens per minute at the window. The scope of possible applications for such tubes is at present relatively unexplored, but many promising possibilities suggest themselves in the fields of sterilization, intracavity therapy, skin therapy, biological research, and photochemical research. Further explorations in these fields will necessitate many measurements of this "soft" x-radiation, for which some of the conventional dosage measuring devices and methods are not suitable. A caution should be registered to the effect that, in the calibration of such apparatus, the usual bakelite thimble chambers should not be employed. Calibration must be carried out by one familiar with the properties of this kind of radiation and the special problems associated with its dosimetry.



To attempt to look a bit into the future, it can be anticipated that processes may be developed to utilize the extremely high intensity of ionizing power which beryllium-window tubes make possible, for sterilization or for the production of various photochemical reactions. In such cases, it will be desired to process the largest possible volume of material in the shortest possible time. Still higher currents and

narrow beam taken out from the diffraction tube, in the form of a 12-degree solid angle cone, includes only about 0.5 per cent of the total. The 40-degree beam of the newer tubes takes in about twelve times more, but that is still only about 6 per cent of the total.

A tube of new design previously described by the author (6) and constructed on an experimental basis makes all of the

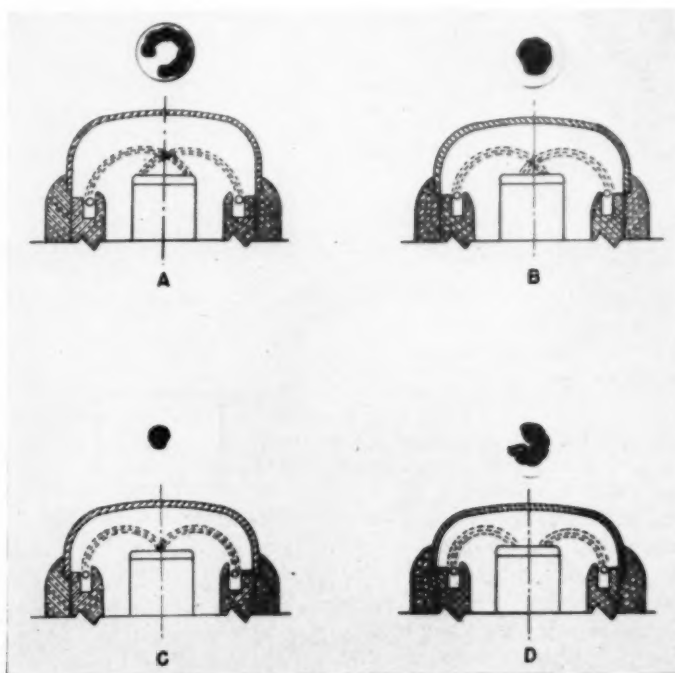


Fig. 8. Diagrams of focusing obtained with domed window tube at various positions of the window with reference to the anode. (Actual pin-hole focalgrams compared with schematic diagrams of electron trajectories.) A. Maximum spacing produces "ring" focus. B. Somewhat closer spacing produces circular focus of large size. C. Spacing adjusted to produce minimum size focus. D. Still closer spacing again results in "ring" focus.

voltages will be advantageously employed for still greater intensities. It will also be desired to utilize all of the radiation generated at the focal spot, not merely the relatively narrow beam required for most diagnostic and therapy applications. The radiation given off from the focal spot radiates in all directions with essentially equal intensity throughout the 180-degree solid angle subtended by the target face. The

radiation available for use in the continuous processing of materials. The principles of this design are shown in Figure 7. The window takes the form of a dome into which the anode protrudes. The filament is in annular form surrounding the anode and located in a plane behind the plane of the target face so that it does not cast a shadow in the hemisphere of radiation. The dome is at cathode potential, and the

resultant electric field in the space between dome and anode is such that the electrons from the filament describe trajectories which terminate on the target approximately as indicated in the diagram in Figure 8.

The formation of such a dome of the malleable beryllium referred to above has been proved to be technically feasible, though not yet reduced to commercial practice. The completion of a commercial design awaits indication of a form properly

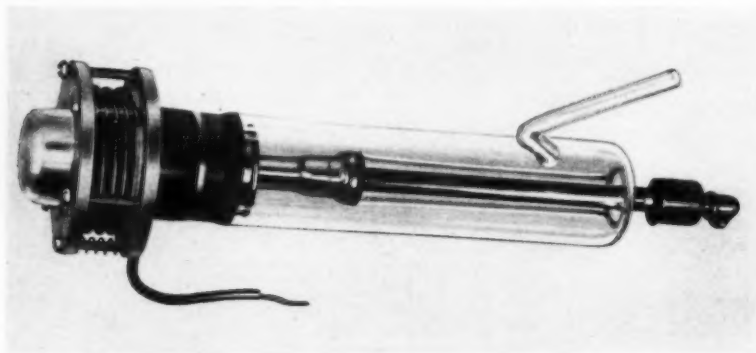


Fig. 9. Experimental tube with domed window permitting 180-degree solid angle x-ray beam. (Courtesy Machlett Laboratories, Inc.)

suitable for desirable processes which are yet to be developed. An experimental model has been constructed operable with a load of 100 ma. at 60 kv. (Fig. 9). Extrapolation of the intensity measurements tabulated above indicates an intensity of approximately 5,000,000 roentgens per minute, which would be available over an area of approximately 25 sq. cm. The uses that can be made of radiation like that are not likely to go long unexplored.

Machlett Laboratories  
Springdale, Conn.

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#### DISCUSSION

**K. W. Stenstrom, Ph.D.** (Minneapolis, Minn.):

Many years ago we searched for suitable window material for x-ray tubes when very soft (long wave length) radiation was studied, and we had a great deal of trouble finding anything useful. We looked at the periodic table of the elements and wished that beryllium were available. Now it is finally produced in thin sheets and it is the ideal material.

Per unit of weight it absorbs about ten times less of the soft x-rays than air; and it thus permits radiation of long wave length to pass out from the tube.

Beryllium, being a metal, can furthermore tolerate a great amount of heat and the window can, therefore, be placed close to the anode where the intensity of radiation is extremely high under the conditions mentioned by the essayist. The short anode-window distance, as well as the low penetrability of the rays makes it difficult to obtain accurate measurements. It seems important, therefore, that special measuring instruments should be designed and recommended for use when the new tubes are being sold.

The new tubes offer several evident advantages over any previously available. For one thing, they can be used over a wide x-ray range, from a very low half-value layer to a relatively high one. One tube can be used for both Grenz-ray therapy and contact therapy, and can thus replace two types of tube.

Other purposes for which these new tubes can be used have already been mentioned, but it may be well to emphasize the advantages they offer for irradiation of bacteria and chemical compounds.

The tremendous intensity will, in a relatively short time, produce reactions which have been very difficult to obtain in satisfactory quantities. It will become much easier to study the changes produced, and it seems probable that some of the products will become of practical importance. It must, however, be remembered that the intensity changes very rapidly, so that the upper layer of the irradiated material will receive much more exposure than the lower portion if it is of any appreciable thickness.

It is an unsettled question whether nearly monochromatic radiation would be of value for therapy. These new tubes offer an opportunity to determine that experimentally. The intensity is high enough so that treatments could be given with a narrow wave-length range if suitable target and filter material were selected. It may, for instance, be of importance to use the characteristic radiation of iron, even though the penetration of this radiation is so slight that it could not be applied to any appreciable depth in the tissues.

The dome type tube, which evidently is not yet completely developed, will undoubtedly have great usefulness for therapy in the future.



# Low-Absorption Roentgen-Ray Measurements from 500 to 1,000 Kilovolts<sup>1</sup>

E. D. TROUT and Z. I. ATLEE

Chicago, Ill.

EARLIER papers (1, 2) by the authors have reported on low-absorption roentgen-ray measurements from 10 to 400 kv. In these cases, the extremely low absorption was made possible by special beryllium-window permanently evacuated tubes. This paper reports an extension of this work to voltages of 500 to 1,000 kv. Roentgen-ray tubes for voltages above 400 kv. usually have not had a glass window for the useful beam of x-rays; rather their exit has been through the wall of a metal anode extension chamber of some sort. This has resulted in high inherent filtration for such tubes and made it especially desirable to obtain physical data at voltages up to 1,000 kv. from a tube having essentially zero filtration.

## BERYLLIUM-WINDOW MILLION-VOLT TUBE

About a year ago it became possible to obtain the desired data, as a result of the experimental construction of a sealed-off multisection million-volt tube with a beryllium window for the reflected beam. The tube used is shown in Figure 1 and aside from the beryllium window is the standard million-volt tube as used extensively with the 180-cycle resonant transformer in a freon-filled tank. The details of this unit have been described elsewhere (3), and more recently a two-million-volt unit of the same fundamental design has been produced (4).

Details of the design of the beryllium-window assembly and water jacket, together with some detail of the tube itself, are shown in Figure 2. The water jacket for cooling the anode wall and target is soldered to the window in such a fashion that the only absorption for this part of the reflected beam is the beryllium window.

In the standard tube the inherent filtration would be the copper wall of the anode, the water, and the two brass jackets, for a total of approximately 6 mm. copper equivalent. (This is indicated in Figure 2 as filtration of the standard tube.) The inherent filtration of the beryllium-window tube is only 3 mm. of beryllium, which will be shown later to be equivalent to about 0.05 mm. of lead. The beryllium window used was 1 1/4 in. in diameter and with some loss for the soldering fillet gave a coverage of a 50 cm. diameter circle at one meter, which was more than ample for all the measurement work as well as radiographic results reported on elsewhere (5).

As mentioned previously, this tube became available nearly a year ago, and the measurements to be reported were made at that time. Since then the tube has been used for other work, and its performance has left nothing to be desired.

## ROENTGEN-RAY MEASUREMENTS

All the measurements were made with a Victoreen condenser type thimble chamber at 100 cm. distance and tube currents varying from 0.1 to 3.0 ma. The kilovoltage was varied at will throughout the 500 to 1,000 kv. range without incident. Because of filament limitation by space charge, a maximum of 1.0 ma. at 500 kv. was used. Absorption data were taken in both copper and lead, since these are the materials normally used as filters at these voltages.

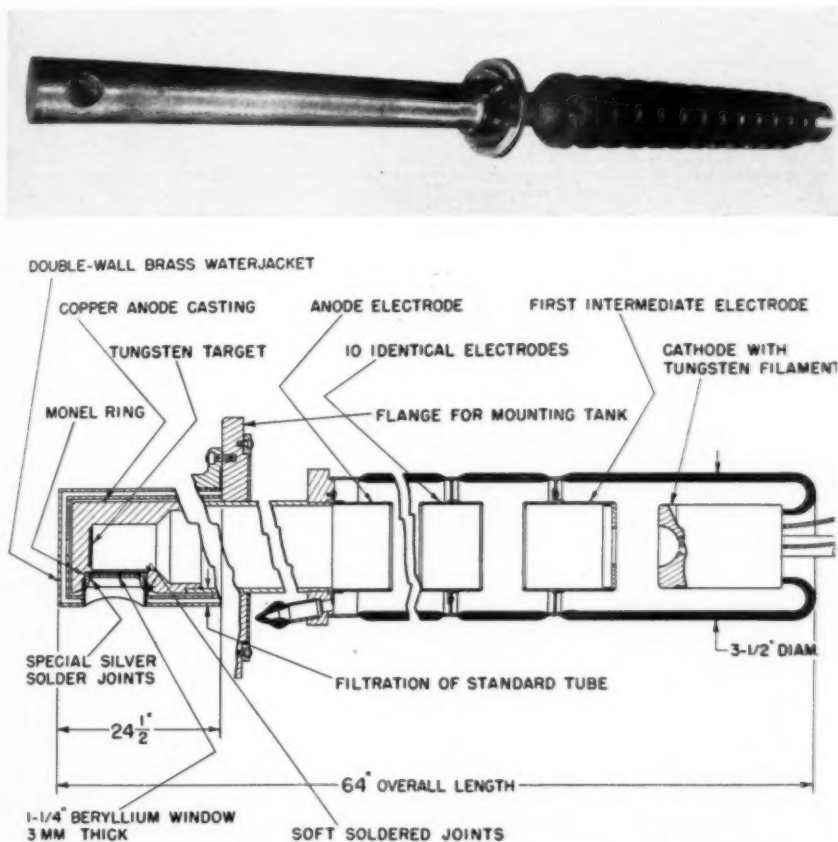
In Figure 3, curves are plotted for transmission data for copper. It will be noted that for voltages up to 750 kv., a few tenths of a millimeter of added copper drops the output rapidly. This, of course, is the measure of the soft radiation present be-

<sup>1</sup> Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

cause of the beryllium window. At 1,000 kv., the slope of the curve is quite flat, differing little from the curve taken with the conventional type of tube, indicating little advantage for the beryllium. This is probably due to the fact that the mass absorption coefficients of all elements

lead is presented in Figure 4. It will be noted that at 1,000 kv. for zero added filtration the half-value layer is 1.1 mm. of lead. In the conventional million-volt tube it is 1.9 mm. of lead.

Figure 5 shows the half-value layers obtained throughout the 500-kv. range of the



Figs. 1 and 2. Beryllium-window million-volt tube and cross-sectional view showing beryllium-window construction.

approach each other at wave lengths of this order. It serves to emphasize the point that in such a tube the thickness of the window is more important than the material from which it is made. This suggests the building of a tube with a thinner window, perhaps by similar water jacket construction with the anode copper extension wall milled very thin.

A similar set of transmission curves for

measurements. At 500 kv. the half-value layer of 0.04 mm. of lead certainly indicates soft radiation.

A comparison of transmission values for lead and copper throughout the 500-kv. range is shown in Figure 6. Here again approach to equality of mass absorption coefficients at the shorter wave lengths is illustrated.

Some idea of the r/min. output actually



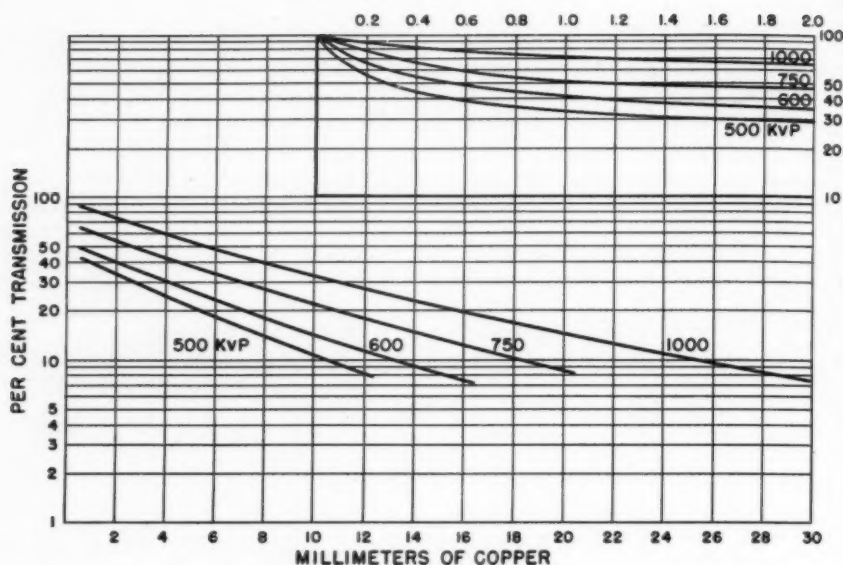


Fig. 3. High-voltage, low-initial-absorption roentgen-ray transmission for copper.

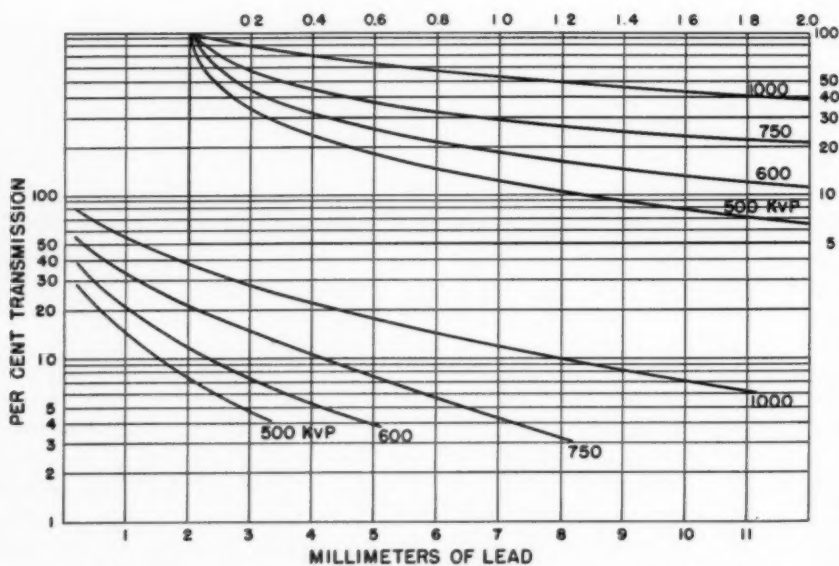


Fig. 4. High-voltage, low-initial-absorption roentgen-ray transmission for lead.

obtained from this tube can be had from Figure 7. At 1,000 kv. and 3 ma., which is full-load rating, and at the usual treatment distance of 50 cm., the output would be 264 r/min. To give some idea as to the intensity of the radiation present at the

closest distance possible for irradiation of small samples, which would be about 2 cm. in contact with the beryllium window, by inverse-square-law calculation we would have  $2,500 \times 66$  (r/min. at 3.0 ma.), or 165,000 r/min. A beam of this intensity

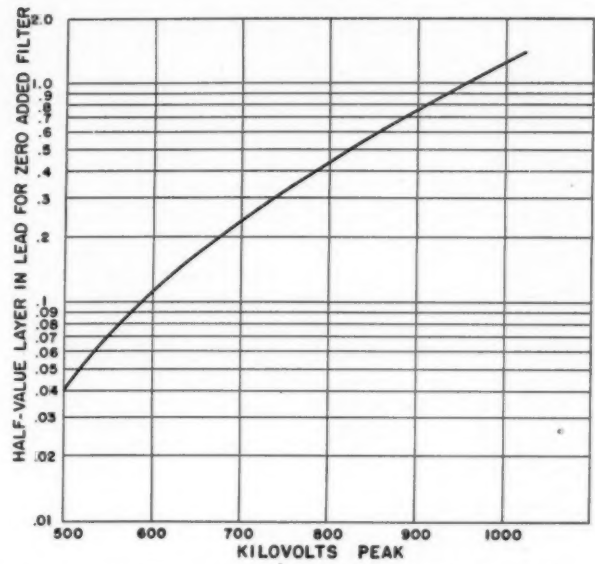


Fig. 5. Half-value layers in lead with low initial absorption for voltages of 500 to 1,000 kv.

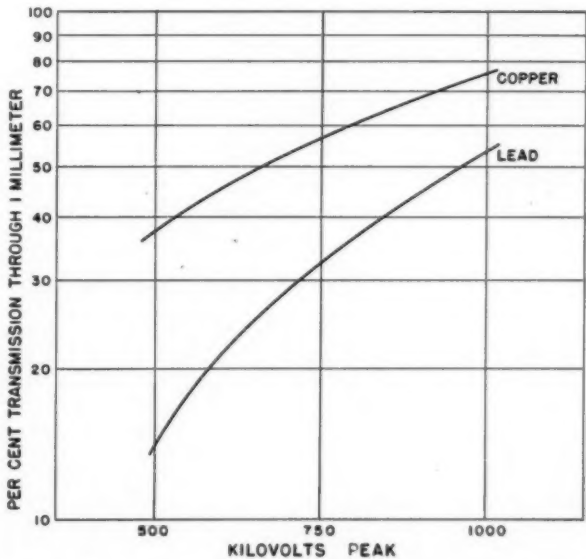


Fig. 6. Per cent transmission through 1 mm. copper and 1 mm. lead for voltages of 500 to 1,000 kv.

might be of interest for biological experimentation.

By calculation from Figure 3, Figure 8 provides the necessary graph for determining the inherent filtration in lead of any

x-ray tube operating in the range of 500 to 1,000 kv. with a measurement of only the half-value layer in lead. The significance of this method of determining the inherent filtration has been amply covered in the

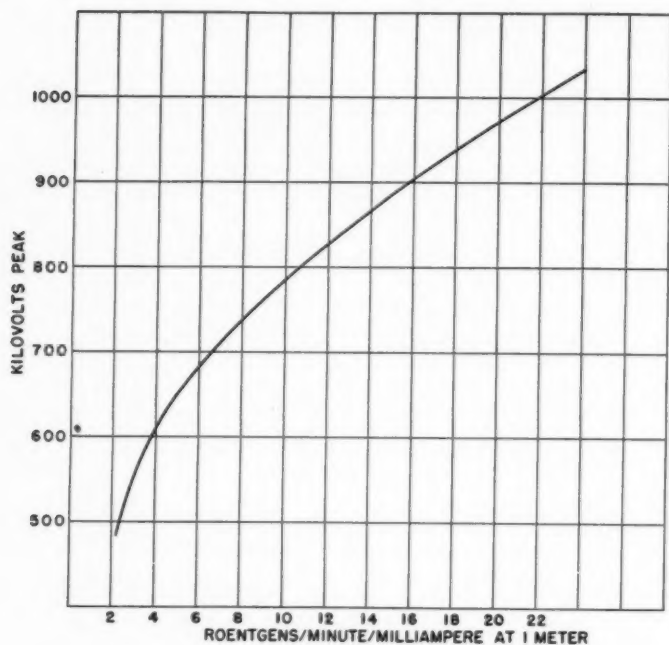


Fig. 7. Roentgen-ray output with low initial absorption for voltages of 500 to 1,000 kv.

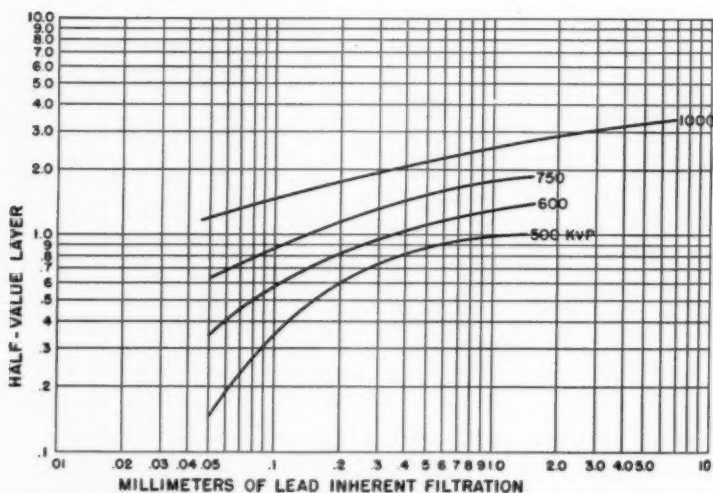


Fig. 8. Graph for determining inherent filtration from half-value layer in lead for voltages of 500 to 1,000 kv

previous papers referred to. Earlier work of Taylor and Singer (6), Behnken and Nitka (7), and Thoraues (8) should be mentioned as contributing to the subject.

#### SUMMARY

1. A million-volt sealed-off multisection tube with beryllium window is described.

2. Roentgen-ray data obtained from the tube on the reflected beam for a voltage range of 500 to 1,000 kv. are presented.

3. A graph is given for determining inherent filtration of any roentgen-ray tube operating at as high a voltage as 500 to 1,000 kv. when only the half-value layer in lead and operating voltage are known.

4. The conclusion is reached that beryllium windows are indicated for tubes operating up to 750 kv., but that at 1,000 kv. and higher the emphasis should be placed on a "thin window" rather than its composition.

Construction of a two-million-volt tube with thinner beryllium window is under way for measurement in the range of 1,000 to 2,000 kv. It was hoped that results obtained with it could have been included in this paper, but unforeseen difficulties prevented.

NOTE: We wish to acknowledge the valuable assistance of R. M. Gager and C. H. Mellor with the measurements. We are also greatly indebted to J. Illingworth for construction of the beryllium-window anode for the tube.

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#### DISCUSSION

Lauriston S. Taylor, Ph.D. (Bethesda, Md.):

This paper by Mr. Trout and Mr. Atlee is very nicely done indeed. We have been hoping in our own laboratory to do a job like this for a long time, because we have felt the real need for it, and I am sure that it is going to be particularly useful in this high-voltage x-ray region. Here, for various reasons, it is necessary to have rather massive and complicated target structure areas and the x-rays, after they pass through these variable windows, may be considerably changed both in their quality and their intensity. Such target mountings can be pretty formidable affairs for various constructional reasons, and, because of the softening and reduction of the x-ray output, it is necessary for economic reasons that we avoid adding any unnecessary filtration to the beam after it leaves the tube.

The question has always been, What is the necessary filter to be added? The data that were presented this morning will provide, I believe, the whole answer to that question. This is a matter of economy, and I really don't take it to be a question of hairsplitting at all.

Some time ago these same workers reported a similar piece of research in the very low-voltage region. This has already demonstrated both its economic and technical usefulness in a really big way, and I see no reason to believe that the work in the very high-voltage region is not going to prove equally useful.

We have been up against the problem in connection with our own million-and-a-half-volt plant. We have had no way of obtaining absorption data for zero or essentially zero filtration between the source of radiation (the target) and the ionization chamber. We have wondered in our own minds just what to do about the question of the filtration that we have had in the water jacket and in the target container. The conclusion of the authors, that for very high voltages the window material is itself immaterial, is very comforting. It is not entirely unexpected, but one always likes to see these things clearly proved before going ahead with a design for an expensive installation. I should like again to congratulate the authors on a good job, well done.

# Experimental Clostridial Infections in Dogs<sup>1</sup>

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THE WORK PRESENTED in this paper represents a chronological summary of approximately six years' experience with clostridial infections in 1,638 dogs. The objectives of the study were to determine the most practical and effective means applicable under conditions of war which would (1) prevent the occurrence of gas gangrene and (2) combat the disease once it had become established.

To accomplish the objectives as stated, the scope of the work was of sufficient magnitude to encompass a study of gas gangrene as produced by several of the most common clostridial organisms both in individual pure culture and mixed culture inocula. The efficacy of a given prophylactic<sup>2</sup> or therapeutic<sup>3</sup> agent was then measured against the virulence of a given infectious agent or agents in the dog with the avoidance of unnecessarily complicating and variable factors. The design of the experiments was such as to minimize trauma and to exclude anesthesia and surgical technics.

The degree and extent of interest and co-operation in the program are denoted by the accompanying list of participating groups and organizations. We are indebted especially to Dr. M. A. Logan and his associate Dr. A. A. Tytell of the University of Cincinnati, who prepared many of the preliminary toxoid preparations and who determined all of the alpha antitoxin titre levels on the dogs utilized in the toxoid experiments.

## EXPERIMENTAL MATERIAL AND PROCEDURES

*Infectious Agents:* The infectious agents used in producing the standardized clostridial

- Participating Groups and Organizations*
- Department of Radiology, University of Rochester  
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- Department of Bacteriology and Immunology, University of Rochester  
C. M. Carpenter, Consultant
- American Cyanamid Co.  
For sulfonamides
- Lederle Laboratories (Division, American Cyanamid Co.)  
For antitoxin and toxoids
- Merck & Co.  
For penicillin
- Study carried out under contract with the Office of Scientific Research and Development.

tridial infections in dogs are listed in Table I. Since the inocula were prepared from media containing chopped meat, the number of organisms per inoculum can be given only in approximation. No attempt was made to differentiate between the vegetative organisms and the readily germinating spores in the various inocula. However, the inocula so used, regardless of the clostridial species, were uniform in respect to the severity of the infections and to the fatalities in the control animals over the several years in which the experiments were carried out.

This consistency in the pathogenicity of

<sup>1</sup> From the Department of Radiology, the University of Rochester School of Medicine and Dentistry, Rochester, N. Y. Presented by Dr. Dowdy at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

<sup>2</sup> Prophylactic as used throughout implies that the treatment agent was given prior to inoculation.

<sup>3</sup> Therapeutic as used throughout implies that the treatment agent was administered subsequent to the inoculation.



TABLE I: INFECTIOUS AGENTS

Nomenclature		Source of Culture	Amount of Inoculum	
Bergey	Medical Texts			
<i>Cl. perfringens</i>	<i>Cl. welchii</i>	S.M.H., † 1939	1.5 ml.	Between 750 million and 1½ billion
<i>Cl. septicum</i>	<i>Cl. septicum</i>	A.T.C.C. †† 8053	1.0 ml.	Between 250 million and 500 million
<i>Cl. novyi</i>	<i>Cl. oedematiens</i>	P. Long	0.5 ml.	Between 50 million and 100 million
		I. Hall, 140		
<i>Cl. bifermentans</i>	<i>Cl. sordellii</i>	I. Hall, 9678	0.2 ml.	Between 70 million and 100 million
Mixed culture 1* ( <i>Cl. welchii</i> , <i>Cl. septicum</i> , <i>Cl. sordellii</i> , <i>Staph. aureus hemolyticus</i> )			0.03 ml.	
Mixed culture 2** ( <i>Cl. welchii</i> , <i>Cl. septicum</i> , <i>Cl. sordellii</i> , <i>Cl. oedematiens</i> , <i>Staph. aureus hemolyticus</i> )			0.03 ml.	
Mixed culture 3* ( <i>Cl. welchii</i> , <i>Cl. oedematiens</i> )			0.2 ml.	

\* Approximately 30 times as virulent as would be expected from simple summation.

\*\* Approximately 40 times as virulent as would be expected from simple summation.

† Strong Memorial Hospital.

†† American Type Culture Collection.

the infectious agents is substantiated by a survey of fatalities in the control animals. In the *Cl. welchii* control animals there was an 86.8 per cent fatality in 129 control dogs in the period from 1941 to 1944. The 25 *Cl. welchii* controls of 1942 showed an 88.0 per cent fatality with an average survival time of 39.5 hours. The 30 *Cl. welchii* controls of 1944 showed a 90.0 per cent fatality with an average survival time of 49.2 hours. This agreement in fatalities was typical of the results obtained with the other clostridial infectious agents used, either singly or in combination (Table II.)

TABLE II: MORTALITY IN CONTROL DOGS (Over Five-Year Period)

Infectious Agent	No. of Dogs	Per Cent Mortality
<i>Cl. welchii</i>	144*	89.5
<i>Cl. septicum</i>	34	100.0
<i>Cl. oedematiens</i>	65	98.4
<i>Cl. sordellii</i>	34	91.1
Mixed culture 1	35	94.3
Mixed culture 2	99	100.0
Mixed culture 3	4	100.0
TOTAL	415*	94.9

Note: Total number of dogs studied (treated and untreated), 1638. There was only one dog out of the 1638 which did not develop the disease from the inoculum.

\* This does not include the 25 control dogs with a smaller inoculum resulting in an 80 per cent mortality.

Douglas' medium (1) containing chopped heart and plugged with vaseline was used both for storage of the clostridia and for cultivation of the infectious inocula. The master cultures were grown at 37° C.

for twenty hours and then stored at 5° C. for at least three months before being used for subculture. The *Cl. welchii* inocula were obtained from a twenty-hour subculture and used directly, without washing. The inocula for *Cl. septicum*, *Cl. oedematiens* and *Cl. sordellii* were obtained from twenty-four-hour transfers of twenty-four-hour master subcultures and were also used directly. When *Staph. aureus* was introduced into the inocula, the organisms were obtained directly from twenty-four-hour unwashed Douglas broth subcultures of a culture which had been stored at 5° C. for one week. The *Staph. aureus* master culture was stored on Douglas agar slants at 5° C.

The amounts of the various inocula were arrived at by a series of tests in which infections were produced which were fatal to the majority of control animals but not so overwhelming as to make them impervious to therapeutic agents.

The mixed inocula were obtained by combining equivalent fractions of the individual inocula and sometimes a small fraction of *Staph. aureus*. The virulence of these mixed inocula was so enhanced that the inoculation dose of the mixtures had to be reduced to one-thirtieth of the size expected from a summation of the individual inocula. Tests proved that this thirtyfold increase in virulence was not due to the presence of *Staph. aureus* but probably brought about by synergistic infectious relationships between

the individual clostridia growing in the infected tissues. The inoculating organisms were always grown in pure culture and combined just prior to inoculation.

**Method of Inoculation:** The inoculum was always combined with one-tenth of its volume of 1:1,000 adrenalin chloride at the time of inoculation. The injection was made by passing a needle (18 gauge) deep into the thigh muscles of the right hind leg until bone was encountered, the inoculation area having been previously clipped and sterilized with iodine and alcohol.

**Recovery of Infectious Agents from Wound Fluid:** Recovery of the infectious agents from the wound fluid could be routinely accomplished in the case of the pure culture infections but was very difficult to perform with any consistency in the case of the mixed infections. Of the numerous methods tried with the mixed infections, the separation of the clostridia in the wound fluid by means of graduated heat shock was found to be the most practical.

**Prophylactic and Therapeutic Agents:** The prophylactic and therapeutic agents were as follows:

1. Roentgen rays
2. Oxygen gas
3. Oxygen gas plus roentgen rays
4. Sulfadiazine plus roentgen rays
5. Sulfadiazine
6. Sulfanilamide
7. Butyryl sulfanilamide
8. Sulfathiazole
9. Penicillin
10. Pentavalent antitoxin
11. Toxoid

The prophylactic agents were administered three hours before introducing the infection, while the therapeutic measures were initiated three hours post infection-inoculation.

The first phase of the work, in which *Cl. welchii* was the only infectious agent used, included treatments with roentgen radiation, intramuscular oxygen, and oral administration of sulfonamides both prophylactically and therapeutically (with the exception of butyryl sulfanilamide, which was given intramuscularly). Sul-

fadiazine also was used therapeutically in combination with intramuscular oxygen and roentgen radiation, and oxygen and roentgen radiation were combined in a series of treatments.

The irradiated dogs received treatments of 100 r (measured in air) once to twice daily for the first group and twice daily for the second group. A description of the treatments has been given in former papers (2, 3). The dogs in the first irradiation group received a smaller infection-inoculation and developed a less severe gas gangrene, as measured by survival rate, than the dogs in the second group.

Oxygen was administered intramuscularly first above the infection site and then into the tissues in the immediate vicinity of the inoculation. The administrations were made twice daily for a period of three days.

Sulfadiazine was administered by stomach tube in doses of 0.5 gm. per kilo of body weight once daily for both the prophylactic and the therapeutic treatments. Sulfanilamide was administered by stomach tube in doses of 0.25 gm. per kilo of body weight twice daily and was used for prophylaxis only. Prophylactic butyryl sulfanilamide was given intramuscularly in doses of 0.25 gm. per kilo of body weight twice daily. These procedures are summarized in Table III. All survivals of the dogs in each experimental phase were based on a ten-day observation period. It was found that this period was entirely adequate to cover late fatalities in the tests.

The second phase comprised studies of the prophylactic value of the sulfonamides against individual clostridial species and against a mixed clostridial infection-inoculum. The therapeutic efficacy of sulfadiazine was also tested against the mixed clostridial infection, and pilot experiments on the prophylactic and therapeutic value of penicillin were carried out (Table IV).

In this second phase the sulfonamides were administered intravenously except for supplementary oral administration when sulfanilamide and sulfathiazole were employed. Sulfadiazine and sulfathiazole were administered intravenously as the so-

dium salts in a 5 per cent solution. Sulfanilamide was administered intravenously *per se* in an 0.8 per cent solution. The supplementary oral doses of sulfanilamide and sulfathiazole were given by stomach tube. The attempt was made to maintain the sulfonamide blood levels as closely between 15 and 20 mg. per 100 c.c. as possible for a period of seventy-two hours. Figures 1, 2, and 3 show the sulfonamide

the blood levels represent the approximate maximal and minimal levels throughout the treatment. As in the first phase, the prophylactic treatments were initiated three hours before infection-inoculation and therapeutic treatments three hours post infection-inoculation.

In the pilot experiments on penicillin, administration of the drug was made by both the intravenous and intramuscular

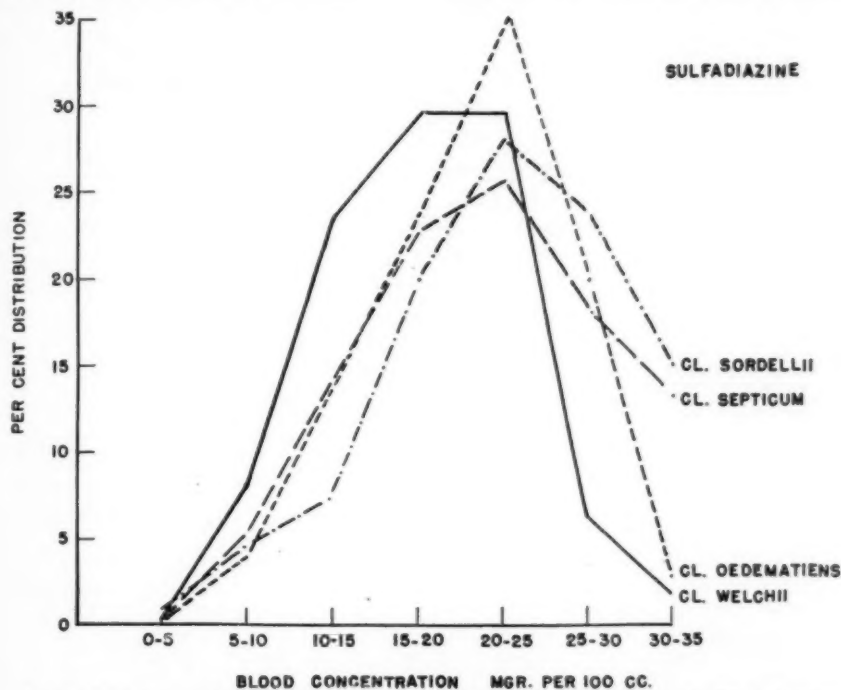


Fig. 1. Blood concentration of sulfadiazine. In this and the following graphs (Figs. 2 and 3), the abscissa gives the blood concentrations in terms of milligrams per cent. The ordinate gives the per cent distribution of the blood levels in the dogs during the course of the treatment.

blood concentrations maintained by the various percentages of the experimental dogs over the course of the treatments. It will be observed that it was possible to maintain a more consistent level with sulfadiazine, even without resorting to supplementary oral dosage, than with sulfathiazole, or sulfanilamide. The blood levels were taken approximately one hour following the initial administration of the sulfonamide and then prior to and immediately following each intravenous drug administration. Thus, in most instances

route. The penicillin doses varied in these pilot tests from 300 units to 2,000 units per kilo of body weight.

The mixed culture used in the second phase contained *Cl. welchii*, *Cl. septicum*, *Cl. sordellii*, and *Staph. aureus* but did not contain *Cl. oedematiens*, since infections with this species were impervious to sulfonamide therapy.

The third phase of the experimental procedure was devoted to therapeutic treatments of clostridial infections produced by mixed culture No. 2 (*Cl. welchii*,

*Cl. septicum*, *Cl. sordellii*, *Cl. oedematiens* and *Staph. aureus*). The definitive agents used were intravenous penicillin and intravenous pentavalent gas gangrene antitoxin (Lederle). The dosage and periods of duration of the treatments are given in Tables V and VII.

Intravenous sodium sulfadiazine was used as an auxiliary agent in certain of the antitoxin and penicillin courses of therapy

to the customary pre-war clinical dosages, were employed. These were only half the value of the later massive doses and were spread out over a considerably longer period. The use of the massive dosage, administered over a shortened period, was arrived at after the preliminary experimentation.

In the "half-treatments" where antitoxin and penicillin were given simul-

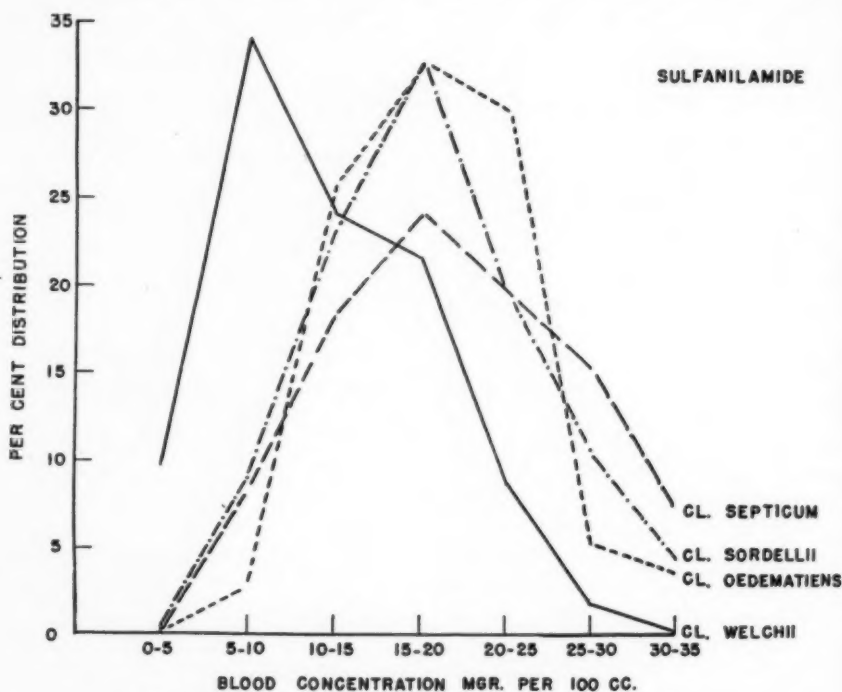


Fig. 2. Blood concentration of sulfanilamide during treatment.

for the reasons that (1) it would act directly upon the invading organism and (2) that its employment would more closely resemble battlefield conditions, where the wounded usually received routine sulfonamide administration. The initial sodium sulfadiazine dose was 0.15 gm. per kilo of body weight and administration was continued to maintain blood levels as nearly as possible between 15 and 20 mg. per 100 c.c.

In a preliminary antitoxin experiment, lower dosages, corresponding fairly well

taneously, the individual periodic doses of both drugs were of the same value as those of the full treatments but administered for only one-half the regular treatment time.

The interval between infection-inoculation and the initiation of antitoxin or penicillin therapy was varied from three hours to twelve hours to test the efficacy of the agents when introduced at early and late stages of the infection.

The fourth phase of the work covers research on the protection afforded by

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toxoid immunization against our standardized experimental clostridial infection in dogs. As mentioned above, this part of the work was carried on in collaboration with the Department of Biochemistry of the University of Cincinnati. The alum precipitated *Cl. welchii* (perfringens) toxoid No. 359H21A, 18.1 Lb., used for all but the preliminary tests, was furnished by Dr. I. S. Danielson of the Lederle division of the American Cyanamid Co.

antitoxin titre range was necessary for this protection. Since the pilot experiments were of necessity of the hit-or-miss variety and since it was possible to carry through only with the more completely standardized *Cl. welchii* toxoid, the results are not here reported.

The toxoid protection used in all of the tests except that in which a booster dose was employed was that afforded by a 1-ml. inoculation of the No. 359H21A *welchii*

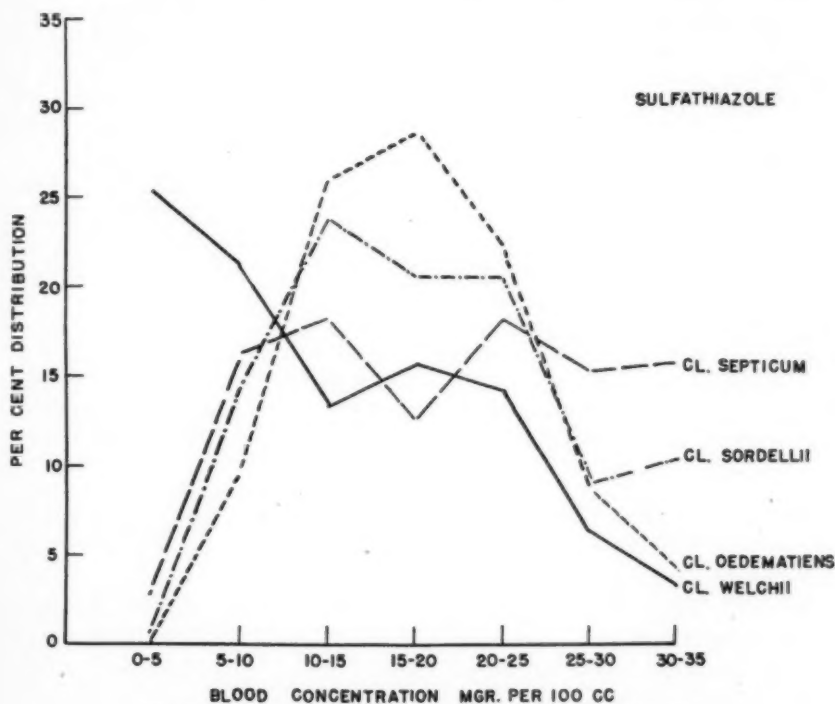


Fig. 3. Blood concentration of sulfathiazole during treatment.

All of the toxoid results reported in the accompanying tables were obtained with protection furnished by *welchii* toxoid against pure *Cl. welchii* infections. Pilot experiments with other *Cl. welchii* toxoids, with *Cl. oedematiens* toxoid, with divalent *Cl. welchii-Cl. oedematiens* 1-1 combination toxoid, and with *Cl. septicum* toxoid were performed for the purpose of discovering whether standardized clostridial infections in dogs could be used to challenge toxoid-induced protection and what

toxoid into the left hind leg of the dog twenty-one days before the infection challenge, which, as always, was introduced into the right hind leg.

The "natural" antitoxin titres referred to in the tables are naturally occurring alpha antitoxin titres present in the dog before immunization. The pre-challenge titres were obtained from blood samples taken immediately before inoculation of the infection-challenge. During the course of the infection, blood samples from the dogs



in two of the series were taken at 12-hour, 24-hour, 72-hour, 5-day, and 10-day intervals to determine the fluctuation of the titre during the course of the infection and to relate this fluctuation to the survival results. (Tables XII and XIII.)

In one of the series of *welchii* toxoid protected dogs, the toxoid protection was supplemented with the regular course of penicillin treatment initiated 12 hours post infection-challenge.

In the booster dose toxoid experiment, the toxoid inoculation was divided into two 0.5 ml. fractions and administered at 10-day intervals for a total immunization period of 20 days. The effect of using one toxoid inoculation to enhance the titre produced by a previous toxoid dose is illustrated in Table XI.

**Control Dogs:** In all of the phases of the experimentation, representative control animals were included to check each infection, and in the case of the mixed infections, controls on the individual clostridia were run along with the controls on the mixed inocula. A statistical analysis of the results obtained in phase two and three has been reported in a previous paper (4).

#### THE INFECTION PICTURE IN THE EXPERIMENTAL DOGS

The gas gangrene infections produced in the experimental dogs were severe and fulminating in character but not so overwhelming as to vitiate the therapeutic measures. The differences in the disease as produced by the several individual clostridial species were as follows:

***Cl. welchii*:** Progress of the infection was very rapid. There were often some toxicity and moderate swelling of the involved leg within three hours after inoculation. Gas could usually be detected by palpation within three to six hours. The overlying skin rapidly took on a bluish-black appearance and serosanguineous seepage was often manifest within twelve hours. Approximately one-half of the control dogs died within the first twenty-four hours. Frank necrosis and sloughing were typical

in the controls that survived for any length of time. The final control mortality approximated 90 per cent.

***Cl. septicum*:** The course of this infection was usually even more rapid than that of *Cl. welchii* infection. Gas was less prominent in the tissues, and pronounced erythema and early necrosis were typical. The mortality in all series of the controls was 100 per cent.

***Cl. oedematiens*:** The course of this infection is relatively slow, particularly in regard to toxicity. The onset of swelling is prompt and it usually becomes extreme before death. Palpable gas was typically absent. The mortality of the control dogs approximated 100 per cent.

***Cl. sordellii*:** The infection was quite similar to that produced by *Cl. welchii* and *Cl. septicum* but was less rapid. There were swelling and discoloration of the involved limb, but little palpable gas was present. The mortality was practically identical with that of the *Cl. welchii* infection.

**Mixed Culture Infections:** The mixed culture infections were characterized by the greatly enhanced virulence already referred to and therefore had to be initiated with much smaller inocula. Each of the mixed culture infections had its particular manifestations as to virulence and course.

Mixed culture No. 1, in which *Cl. oedematiens* was omitted, produced a slowly developing infection with only 20 per cent dead in the first twenty-four hours and an average survival time of fifty-six hours.

Mixed culture No. 2, which included *Cl. oedematiens*, was considerably more rapid in its effect than No. 1, with an average survival time of thirty-four hours. The mortality was also slightly higher than with No. 1 for the same amounts of inocula.

The infections produced by these mixed inocula were a composite picture of the infections produced by the individual inocula. Thus, with mixed culture No. 2, there were the rapid onset, considerable gas production, frequent pockets of serosanguineous fluid characteristic of *Cl.*

TABLE III: FIRST PHASE: X-RAY, OXYGEN, AND ORAL PROPHYLAXIS  
(Infectious Agent: *Cl. welchii*)

	No. of Dogs per Experiment	Per Cent Survival
First x-ray group (smaller infection-inoculation)	25	36
Second x-ray group	25	16
Intramuscular oxygen	25	24
Intramuscular oxygen and sulfadiazine	10	10
Intramuscular oxygen and x-ray	25	28
Prophylactic sulfadiazine (0.5 gm./k.S.T. 1 X D)	25	88
Prophylactic sulfanilamide (0.25 gm./k.S.T. 2 X D)	15	60
Prophylactic butyryl sulfanilamide (0.25 gm./k.I.M. 2 X D)	10	30
Therapeutic sulfadiazine (0.5 gm./k.S.T. 3 hr. P. I.)	25	28
Therapeutic sulfadiazine and x-ray	25	12
Control dogs: no treatment	117*	16.2

\* This includes a group of 25 control dogs having a smaller inoculum resulting in a 20 per cent survival.

III. It should be noted that part of these experiments are prophylactic and part therapeutic. None of the therapeutic results is highly significant as to the ratio of survivals between the control dogs and treated animals.

The differences between the percentages of survivals in the first and second x-ray groups are probably due to the smaller infection-inoculation in the first group, which would result in a more slowly developing infection and therefore one which might be more amenable to x-ray therapy. While the difference in fatalities between the series treated with x-ray only and that in which a combination of therapeutic sulfadiazine and x-ray treatment was used is slight, this result coincides with the supposition that x-ray and the sulfonamides are incompatible.

TABLE IV: SUMMARY OF RESULTS WITH EXPERIMENTAL CLOSTRIDIUM INFECTION IN DOGS, JAN. 1, 1942-JAN. 31 1943: SECOND PHASE  
(All percentages based on ten-day survivals)

	Prophylactic						Therapeutic	
	Cl. welchii	Cl. septicum	Cl. oedematiens			Cl. sordellii	Mixed Culture*	Cl. oedematiens (Long's)
			Long's Culture	Hall's Culture	Long's Reduced Inoculum			
Sulfadiazine	92%	72%	4%	0	36%	80%	88%	48%
Sulfathiazole	44%	28%	0			32%	80%	
Sulfanilamide	20%	0	0			40%	48%	
Penicillin (pilot experiments)			71.4%†					100%†
Controls: no treatment	12%	0	4%	0	20%	12%	6.6%	0†

\* Mixed Culture: *Cl. welchii*, *Cl. septicum*, *Cl. sordellii*, *Staph. aureus* hemolyticus.

† Less than 25 dogs per group (pilot experiments).

*welchii*, and frequently the pronounced erythema of *Cl. septicum* infection, particularly in the control dogs; as the infection progressed, the almost brawny swelling characteristic of the later stages of *Cl. oedematiens* infection was superimposed on the softer swelling; the putrefactive odor of *Cl. sordellii* was also characteristic of the infection. In the later stages, a pus-like fluid associated with *Staph. aureus* was present.

#### RESULTS

**First Phase:** The results for the first phase of the work are summarized in Table

**Second Phase:** Table IV shows the efficacy of prophylactic treatment with the sulfonamides against the individual clostridial infections and against mixed culture No. 1. It might be pointed out that intravenous sulfadiazine maintained at blood levels approximating 15 to 20 mg. per 100 c.c. gave about the same survival rate as prophylactic oral sulfadiazine administered to produce blood levels between 3 and 8 mg. per 100 c.c. The higher blood level of sulfadiazine, however, produced a significantly greater therapeutic survival rate against mixed culture No. 1 than the oral sulfadiazine used therapeutically pro-

TABLE V: THIRD PHASE OF STUDY: THERAPEUTIC PENICILLIN DOSAGE  
(Seventy-Two Hour Treatment Period)

1. First two doses at 2-hour intervals: 2,000 Oxford units per kilo body weight.
2. Third through 24th dose at 3-hour intervals: 1,000 Oxford units per kilo body weight.
Total dosage for 72 hours: 26,000 Oxford units per kilo body weight.
10-kilo dog: Total dosage, 260,000 Oxford units
70-kilo man: Total dosage, 1,820,000 Oxford units

duced against *Cl. welchii* infection. The time element is not comparable in the two instances, for when the sulfadiazine was given orally three hours post-inoculation, it required upward of four hours for the drug to reach maximum levels in the blood stream.

A careful study with two strains of *Cl. oedematiens* has shown that the sulfonamides are ineffectual against this infection. The pilot experiments with penicillin suggested its use in the therapeutic studies of phase three.

While sulfadiazine proved to be far superior to the other sulfonamides as a prophylactic agent, its failure to counteract *Cl. oedematiens* infections makes its value under battle conditions questionable (5).

The incidence of pathogenic clostridia in 164 known cases of gas gangrene in the Middle East Theatre is given by MacLennan (6). The incidence in 17 cases studied on the Italian front is cited by MacLennan and MacFarlane (7).

Third Phase: *Cl. oedematiens* was included in mixed culture No. 2 used in the third phase to test the therapeutic efficacy of penicillin and pentavalent antitoxin.

The data in Table VI demonstrate the effectiveness of therapeutic penicillin in combating the clostridial infections in early stages of the disease. As the disease develops, penicillin becomes progressively less effective. This is presumably due to its inability to control the toxemia which had established itself in twelve hours after infection-inoculation.

An *in vitro* test was set up to study the possible inactivation of penicillin by the direct action of *Cl. welchii* toxin. Dilutions of alpha toxin to produce final con-

centrations of from 175 to 7 M.L.D. were mixed with equal volumes of normal saline containing one unit of penicillin. These were tested against control dilutions of the toxin and saline, and penicillin and saline. Under the conditions of the test, the toxin was found to produce no direct action upon the penicillin.

TABLE VI: THERAPEUTIC AGENT: PENICILLIN  
(DEFINITIVE)  
(Infections Agent: Mixed Culture 2)

Therapeutic Agent	No. of Dogs per Experiment	Per Cent Survival
Penicillin: 3 hr. post-inoculum	25	100
Penicillin: 6 hr. post-inoculum	25	88
(Na Sulfadiazine: 3 hr. post-inoculum, 1 dose)		
Penicillin: 12 hr. post-inoculum	6	0.0
Penicillin: 12 hr. post-inoculum	12	8.3
(Na Sulfadiazine: 3 hr. post-inoculum, 1 dose)		
Penicillin: 3 hr. post-inoculum	6	100
(Na Sulfadiazine: 3 hr. post-inoculum for 72 hr.)		
No Inoculum; Penicillin and Na Sulfadiazine for 72 hr. (compatibility test)	2	100
Control dogs: No treatment. Mixed culture 2	99	0.0
Control dogs: No treatment. Individual cultures which compose mixed culture 2	36	0.0

The concentration of penicillin in the blood of representative infected dogs was tested from time to time by a filter paper disk modification of the Oxford cup method (8). This concentration was found to be rather variable with individual dogs and to diminish quite rapidly, indicating that the two- or three-hour administration intervals were necessary.

Sulfadiazine was found to be compatible with penicillin in gas gangrene therapy. However, its inclusion in the treatment was of doubtful value.

The therapeutic efficacy of antitoxin as summarized in Table VIII was excellent, whether administered early or late in the progression of the mixed infection. This, however, was true only of the massive doses administered over a shortened period.

Antitoxin was not as effective as penicil-

TABLE VII: PENTAVALENT ANTITOXIN  
(Massive Dosage. Six-Hour Treatment Period)

1. <i>Cl. welchii</i> antitoxin: 2,000 units/kilo body weight*
2. <i>Cl. septicum</i> antitoxin: 2,000 units/kilo body weight*
3. <i>Cl. oedematis</i> antitoxin: 300 units/kilo body weight*
4. <i>Cl. sordellii</i> antitoxin: 300 units/kilo body weight*
5. <i>Cl. histolyticus</i> antitoxin: 600 units/kilo body weight*

Total dosage in 6 hours

10-kilo dog, 80,000 *Cl. welchii* antitoxin six hours (others in vial proportions).70-kilo man, 560,000 *Cl. welchii* antitoxin in six hours.

\* These dosages were given at two-hour intervals for 4 doses.

lin in combating the local sepsis of gas gangrene. A combination of the two definitive agents appeared to approach the ideal treatment even when antitoxin and penicillin administrations were initiated at a late stage of the disease and limited to a "half-treatment" by each agent. The 88 per cent survival (Table VIII) of the combined antitoxin and penicillin group would have been somewhat higher except for the death of two dogs in that group from anaphylactoid effects. Inclusion of sulfadiazine in the antitoxin treatments appeared to be of little value.

The prophylactic efficacy of penicillin when administered early in war casualties is illustrated in a report by Fisher, Florey, Grimson, and Williams (9). The value of large antitoxin dosage as early as possible in the disease, with adequate accompanying surgical measures, is reported by MacLennan and MacFarlane (10).

**Fourth Phase:** The experiments on the protection afforded by *Cl. welchii* toxoid No. 359H21A against the standardized *Cl. welchii* infection brought out the evaluation of the critical alpha antitoxin level necessary for immune protection, the value of late penicillin therapy in combination with the toxoid protection, the effect of the booster toxoid dose in establishing greater immunity, the relation of the titre level during the course of the infection to recovery, and the comparison between adequate therapeutic antitoxin and adequate toxoid protection. These results are presented in Tables IX-XIV.

It was shown that an alpha antitoxin level of less than 0.1 titre units per ml. of blood produced only an approximate 50 per cent survival as against an approximate 100 per cent survival when the titres were 0.1 unit or over at the time of infection.

TABLE VIII: THERAPEUTIC AGENT: ANTITOXIN  
(DEFINITIVE)  
(Infectious agent: Mixed Culture 2)

Therapeutic Agent	No. of Dogs per Experiment	Per Cent Survival
Antitoxin: 3 hr. post-inoculum (smaller customary clinical dose)	8	62.5
Antitoxin: 3 hr. post-inoculum (massive dose given within 6 hr.)	25	88.0
Antitoxin: 12 hr. post-inoculum	25	92.0
(Na Sulfadiazine: 3 hr. post-inoculum, 1 dose)		
Antitoxin: 12 hr. post-inoculum	25	84.0
(Na Sulfadiazine: 3 hr. post-inoculum for 72 hr.)		
Antitoxin and Penicillin: 12 hr. post-inoculum; half treatment by each agent	25	88.0
(Na Sulfadiazine: 3 hr. post-inoculum, 1 dose)		
Control dogs,* No treatment. Mixed culture 2	99	0.0
Control dogs,* No treatment. Individual cultures which compose mixed culture 2	36	0.0

\* Control dogs, same as for penicillin.

tion-challenge. There was a direct relationship between the height of the titre level and the protection against severe infection.

Penicillin therapy initiated comparatively late in the infection (twelve hours post-infection challenge) did not lower the fatalities in the group of dogs having less than 0.1 alpha antitoxin titres. This result agrees with those obtained in the third phase, in which it was found that penicillin does not have much effect when administered late in well developed clostridial infections unless it is accompanied by adequate antitoxin protection. The penicillin, however, helped reduce the severity of the infection in the dogs having 0.1 titre unit or more of alpha antitoxin. The concentration of penicillin in the dogs' blood ranged from an average of from 2.0



TABLE IX: FOURTH PHASE: EVALUATION OF CRITICAL ALPHA ANTITOXIN TITRE LEVEL  
(85 Dogs. Infectious Agent: *Cl. welchii*)

Pre-Infection Challenge Alpha Antitoxin Titre	No. of Dogs	Degree of Infection			Per Cent Survival
		Slight	Moderate	Severe	
Group I: Titre less than 0.1	25	3	3	19	48
Group II: Titre from 0.1 to 0.5	29	8	13	8	96.5
Group III: Titre from 0.5 to 5.0	31	15	14	2	96.7

TABLE X: COMBINATION OF TOXOID PROTECTION AND PENICILLIN\* THERAPY

Pre-Infection Challenge Alpha Anti- toxin Titre	No. of Dogs	Degree of Infection			Per Cent Survival
		Slight	Moderate	Severe	
Toxoid only					
Group I: Titre less than 0.1	6	1	1	4	50.0
Group II: Titre from 0.1 to 0.5	13	3	4	6	92.3
Group III: Titre from 0.5 to 5.0	5	2	2	1	100.0
Toxoid plus penicillin					
Group I: Titre less than 0.1	5	0	1	4	40.0
Group II: Titre from 0.1 to 0.5	10	4	4	2	100.0
Group III: Titre from 0.5 to 5.0	10	6	4	0	100.0

\* Twelve hours post-infection challenge.

TABLE XI: EFFECT OF BOOSTER DOSE OF TOXOID

Pre-Infection Challenge Alpha Anti-toxin Titre	No. of Dogs	Degree of Infection			Per Cent Survival
		Slight	Moderate	Severe	
Single 1 ml. dose (24 dogs)					
Group I: Titre less than 0.1	6	1	1	4	50.0
Group II: Titre from 0.1 to 0.5	13	3	4	6	92.3
Group III: Titre from 0.5 to 5.0	5	2	2	1	100.0
Booster dose. Two 0.5 ml. doses at 10-day intervals (12 dogs)					
Group I: Titre less than 0.1	1	0	0	1	100.0
Group II: Titre from 0.1 to 0.5	2	1	1	0	100.0
Group III: Titre from 0.5 to 5.0	9	7	2	0	100.0

TABLE XII: TYPICAL ALPHA ANTITOXIN LEVELS (1 ML. TOXOID INOCULATION)

Dog No.	Type of Level	Alpha Antitoxin Titres							Result
		Natural Titre	Pre-Challenge Titre	During Course of Infection Challenge					
				12 hr.	24 hr.	72 hr.	5 days	10 days	
X73	Fluctuating	Less than 0.1	Less than 0.1	0.1-0.2	Less than 0.1	Less than 0.1	0.5	1.0-2.0	Recovered
X68	Fluctuating	0.2-0.5	2.0-5.0	2.0-5.0	1.0	1.0-2.0	More than 5.0	More than 5.0	Recovered
X54	Steady	Less than 0.1	Less than 0.1	Less than 0.1	0.2-0.5				Died in 29 hr.
X62	Steady	Less than 0.1	0.2-0.5	0.2-0.5	0.2-0.5	0.2-0.5	1.0-2.0	More than 5.0	Recovered
X29	Steady	Less than 0.05	1.0-2.0	1.0-2.0	1.0-2.0	0.5-1.0	1.0-2.0	1.0	Recovered
X53	Continuous rise	Less than 0.1	Less than 0.1	0.2	0.2-0.5				Died in 72 hr.
X56	Continuous rise	Less than 0.1	Less than 0.1	0.1-0.2	0.1-0.2	0.2-0.5	2.0	More than 5.0	Recovered
X66	Continuous rise	Less than 0.2	1.0-2.0	1.0-2.0	2.0-5.0	2.0-5.0	More than 5.0	More than 5.0	Recovered



TABLE XIII: RELATION OF ALPHA ANTITOXIN TITRE CURVES TO PROGRESS OF THE INFECTION

Pre-Infection Challenge Alpha Anti-toxin Titre	No. of Dogs	State of Titre Level During Course of the Infection		
		No. of Dogs	Degree of Infection	Per Cent Survival
Group I: Titre less than 0.1	11	Fluctuating..... 2	Severe.....	50.0
		Steady..... 4	Severe.....	25.0
		Continuous rise.... 5	Moderate....	60.0
Group II: Titre from 0.1 to 0.5	25	Fluctuating..... 14	Moderate....	92.8
		Steady..... 5	Moderate....	100.0
		Continuous rise.... 6	Slight.....	100.0
Group III: Titre from 0.5 to 5.0	13	Fluctuating..... 9	Slight.....	100.0
		Steady..... 3	Slight.....	100.0
		Continuous rise.... 1	Slight.....	100.0

TABLE XIV: COMPARISON OF THERAPEUTIC ANTITOXIN AND TOXOID PROTECTION

Definitive Agent	No. of Dogs	Degree of Infection			Per Cent Survival
		Slight	Moderate	Severe	
Inadequate therapeutic antitoxin dosage (4,000 units/k.)	8	1	1	6	65.5
Toxoid-produced subcritical alpha antitoxin titres	25	3	3	19	48.0
Adequate (massive) therapeutic antitoxin dosage (8,000 units/k.)	25	9	9	7	88.0
Toxoid-produced alpha antitoxin titres above critical level	60	23	27	10	96.6

to 2.5 Oxford units per ml. at the maximum levels taken fifteen minutes after administration of the penicillin to minimum levels of from 0.062 to 0.125 unit per ml. taken just before the administration of a repeat dose of penicillin (8).

The booster toxoid dose produced the greatest protection for the amount of toxoid used both as to the pre-challenge titre established in the dogs and their resistance to and recovery from the infection. There was a 100 per cent survival in this group.

The alpha antitoxin curves during the progress of the infection bore a direct relationship to the recovery of the infected animals. These titre fluctuations may be thought of as interrelationships between such factors as the degree of pre-challenge titre, the poise of the antitoxin immunity, the production of alpha toxin by the infection invasion, and the response of the immune system to antitoxin production from the stimulus provided by this invasion toxin. A continuous rise in the titre levels enhanced the probabilities of survival and the speed of recovery from the infection.

While the toxoid protection has been measured in terms of the alpha antitoxin

levels, the immunity so defined might be considered representative of immune protection against other toxins produced by *Cl. welchii* infections. The theta antitoxin production from immunity established with *Cl. welchii* toxoid No. 359-H21A and the rise of the levels of theta antitoxin during the course of the infection were measured in representative dogs and found to be fairly comparable to those of alpha antitoxin.

A comparison of therapeutic antitoxin and toxoid protection indicates that these methods of combating the infection have quite similar effects. When the alpha antitoxin level was above the critical 0.1 unit, the toxoid immunization produced a slightly higher percentage of survival and a somewhat superior recovery from local sepsis and toxicity of the infection.

#### EFFECT OF LIVER SUPPLEMENT ON THE ANTITOXIN RESPONSE IN EXPERIMENTAL DOGS

An interesting relationship between diet and the pre-challenge titres produced by *welchii* toxoid was observed during the experiments on toxoid immunization (Table XV). Circumstances prevented

TABLE XV: RELATION OF DIET TO PRE-CHALLENGE TITRES PRODUCED BY WELCHII TOXOID

Distribution of Alpha Titres	Less than 0.1 u.	0.1 u.-0.5 u.	0.5 u.-2.0 u.	2.0 u.-5.0 u.	Total Survival
Series I: 24 dogs. No liver supplement	13 dogs	3 dogs	4 dogs	4 dogs	66.6%
Distribution in titre groups	54.2%	12.5%	16.6%	16.6%	
Survival in titre groups	46.2%	100.0%	100.0%	75.0%	
Series II: 24 dogs. Liver supplement	5 dogs	14 dogs	4 dogs	1 dog	83.3%
Distribution in titre groups	20.8%	58.3%	16.6%	4.2%	
Survival in titre groups	40.0%	93.5%	100.0%	100.0%	
Series III: 25 dogs. Liver supplement	5 dogs	10 dogs	8 dogs	2 dogs	88.0%
Distribution in titre groups	20.0%	40.0%	32.0%	8.0%	
Survival in titre groups	40.0%	100.0%	100.0%	100.0%	

the use of a liver supplement to the diet in the first series of dogs immunized with *Cl. welchii* toxoid No. 359H21A. It was later observed in the animals receiving the liver supplement that there was a 2.6-fold decrease in the number with inadequate titre protection (under 0.1 unit). Except for differences in diet, the same methods of immunization were used for each series. The dogs were obtained from the same source of supply, received the same handling, had similar distribution as to size, age, and breed, and the time of the year in which the experiments ran was from late June to early October. As far as our data indicated, there was no correlation between worm infestation in these dogs and titre production. In earlier pilot experiments in which a cooked horse-meat supplement had been added to the diet, no differences in antitoxin response were apparent.

The dog meal fed routinely in the series without the liver supplement, and continued as a basic feed in the liver supplement experiments, was a typical dog chow (Field Trial Dog Chow). This meal had been used over the course of several years and had kept the caged dogs in good condition, usually producing gains in weight. The liver supplement used was pig's liver in a relatively fresh state, prepared for feeding by simmering whole livers for approximately one hour and grinding; it was fed along with the broth. The dogs of average size received about one-half pound of the cooked and ground liver, with a proportionate amount of broth mixed with the dog meal, spread out over the feedings for a week.

An examination of Table XV will show that a certain number of the dogs in Series I, which did not receive the liver supplement still developed high titres on the regular dog chow. The effect of the liver supplement, therefore, was that of materially decreasing the number of dogs which could not develop adequate titres on the dog chow diet. This consideration suggests that the dogs with the inadequate titres may have failed to utilize a dietary element from the dog meal, an element which the liver supplement supplied to the later series. Topley and Wilson (11) cite a few examples in which vitamin variations in diet are reported to have modified antibody response. Hartley (12) describes experiments in which an addition of cabbage to the basal bran and hay diet of guinea-pigs produced a greater degree of immunity from diphtheria-formol toxoid than was obtained with a mangold supplement to the basal diet. In another publication, however, Hartley (13) found that a restricted diet did not affect the response of previously immunized guinea-pigs to fresh toxoid injections.

The relationship between diet and immunity is also affected by an adequate supply of protein in the diet to maintain the synthesis of antibody-globulin and to conserve the "intracellular globulin matrix" (P. R. Cannon, 14). Madden and Whipple (15) have shown that diet regulates globulin production in dogs. Cannon (16), in a later publication, showed that rabbits made hypoproteinemic by low-protein diets had a lessened capacity to produce agglutinins.

There was no evidence that the dogs used in the above experiments were hypoproteinemic, and as a whole they gave the appearance of being well nourished both with and without the liver supplement. This evidence on the relationship of diet to antitoxin production is presented as being suggestive of further investigation rather than as evidence that such relationships exist. It should be particularly pointed out that this diet relationship was apparent only in dogs with the relatively low titres produced by a single one-ml. toxoid dose.

#### PATHOLOGY

For a detailed account of the pathology resulting from clostridial infections in dogs, the reader is referred to a previous publication limited to that subject (17). We shall confine ourselves at this time to a brief summary of the findings.

Careful pathological studies were conducted on 26 untreated control dogs and on 43 receiving one or more therapeutic or prophylactic agents, a total of 69 dogs. Autopsies were performed on representative animals selected from each experimental group as soon after death as possible. Most of the recovered dogs were sacrificed by intravenous nembutal and chloroform. All the organs except the brain and spinal cord were examined routinely. In four dogs dying of the infection, the brain and spinal cord were studied with negative results. In the control animals, the tissues and organs most involved were the muscles at the site of inoculation, the heart, and the liver, in the order named. The kidneys in both the control and treated animals were uniformly free from hemorrhage and necrosis.

The control dogs subjected to histologic examination were inoculated with individual cultures of *Cl. welchii*, *Cl. septicum*, *Cl. oedematiens*, *Cl. sordellii*, or a mixture of these four organisms plus *Staph. aureus* (mixed culture No. 2). In general, the animals in the control group using the mixed culture No. 2 revealed a more severe damage than did the animals receiving a

pure strain of one of the clostridial organisms. It was impossible to determine any difference in the degree of damage resulting from the disease when produced by the various individual pure culture clostridia inocula. The pathology studies confirmed our clinical impression, in that they showed uniformly a severe infection with extensive damage at the site of the inoculation.

Microscopically, the muscle in the region receiving the inoculum was largely replaced by a diffuse mass of fibrin and degenerated red blood corpuscles. Many of the remaining muscle fibers revealed a loss of nuclei. The changes in the heart muscles were scattered throughout and consisted of areas of moderate to severe fragmentation of the muscle fibers with swelling, loss of striations, pallor, fine and coarse granular degeneration. Frequently scattered areas of Zenker's "waxy degeneration" of the muscle fibers were seen. In all instances the liver was markedly engorged with red blood corpuscles. Small areas of focal necrosis were noted in some instances.

In the successfully treated animals there was excellent recovery of the inoculated site. Some of the involved legs were practically normal in gross and microscopic appearance. The heart revealed only an occasional area of old necrosis with good organization. The few dogs dying as a result of the disease, despite prophylactic or therapeutic measures, manifested severe cardiac damage. In several, the liver was undamaged. Two of the dogs receiving antitoxin therapy died an anaphylactoid death.

#### CLINICAL APPLICATIONS

It has been pointed out that gas gangrene as produced in the dog is similar in character to a *fulminating* infection as seen in man. In general, the swelling and necrosis in the dog remain confined to the involved leg and the immediate surrounding tissues of the lower abdomen. The course of the disease is rapidly and progressively downhill in a very high percentage of the untreated animals as manifested

by a severe local reaction and a progressive general toxemia. Death presumably results from cardiac failure.

The dissimilarity in the production of the disease from that of the naturally occurring infection in man must be pointed out. The clinical disease as seen in man usually results from a few spores of one or more strains of clostridial organisms being carried into or beneath the skin with the accompaniment of clothing, dirt, or other contamination, as a result of some minor or major trauma. The trauma *per se* may be of sufficient magnitude to endanger life without a complicating fulminating infection. The vascularity of the involved part subsequent to the trauma is of vital importance and may in itself dictate the extent of surgical intervention. Irrespective of the injury, the spores are introduced in comparatively small numbers unaccompanied by exotoxins. The spores require a variable period to germinate into vegetative forms and, in turn, must form their exotoxins *in situ*. This sequence of events permits a variable length of time to intervene between contamination of the wound with the clostridial spores and the onset of the disease clinically. In some instances this incubation period may be as long as forty-eight to seventy-two hours. In the disease as produced in the dog, the variable and complicating factor of major trauma has been circumvented. The trauma is reduced to a needle puncture wound. The organisms injected are in large numbers (Table I) in the vegetative and spore state and are accompanied by a certain amount of exotoxin (unwashed cultures). It can readily be seen that in the dog the disease has its onset at the time of inoculation and without treatment usually progresses rapidly to a mortality of approximately 50 per cent within twenty-four to twenty-six hours.

Bearing these differences in mind, it is justifiable to point out certain clinical applications of this study. It has been demonstrated that prophylactic sulfadiazine when given systemically (orally or intravenously) in the presence of an ade-

quate circulation at the site of the primary involvement results in a high degree of protection against experimental infections in dogs produced by pure strain inocula of *Cl. welchii*, *Cl. septicum*, and *Cl. sordellii* but is ineffective against two different pure strain inocula of *Cl. oedematiens* (Table IV). It seems reasonable, under similar conditions, to assume a similar prophylactic value in man. During the latter half of this study we have seen only an occasional patient with gas gangrene. Perhaps the rather general prophylactic use of the sulfonamides has brought about this reduction in civilian practice. Once the infection was established experimentally, we found sulfadiazine rather ineffective as a therapeutic agent (Table IV). We would expect its clinical therapeutic value to be equivocal.

The study of penicillin was limited to its therapeutic aspects. In our hands it was found to be extremely effective when given early, prior to severe toxemia. It was effective against the disease when produced by mixed culture No. 2 or by a pure strain inoculum of *Cl. oedematiens*. As would be expected, penicillin had no antitoxic effect and when given relatively late in the disease was not remarkably effective. The best results were obtained when massive doses were instituted prior to general toxemia (Table V).

Polyvalent antitoxin given in massive doses, over a period of six hours, proved to be effective when treatment was instituted as late as twelve hours after inoculation (Table VIII). Under these conditions it was quite remarkable as a therapeutic measure. In smaller doses it was unimpressive. In massive doses it did not prevent a variable degree of local sepsis. The combination of polyvalent antitoxin and penicillin was most effective in combating local sepsis and general toxemia. Clinically we can postulate that *large* doses of polyvalent antitoxin plus *large* doses of penicillin should be an effective means of treating the established clinical infection in man, *provided* the circulation is adequate at the site of the primary infection.



Residual cardiac damage in man, as reported by Sewell (18) and experimentally demonstrated in dogs, indicates that the sooner adequate antitoxin therapy is instituted, the less likelihood there is of a residual cardiac injury. Care must be taken to test the patient for sensitivity to the antisera. Desensitization must precede the administration of therapeutic amounts of antitoxin.

Unpublished data<sup>4</sup> indicate that human toxoid immunization with *Cl. welchii* toxoid will produce alpha antitoxin titre of 0.1 unit, or more, per ml. of blood. Experimentally we found this to be the critical level (Table IX). The infection-challenge dose given the dog exceeds by far that which would normally be encountered in man. We should expect adequate protection in man by this method of immunization.

The clinical measures indicated from the discussion are in no way contrary to the dictates of good surgery. They are not meant to replace surgical measures as indicated in the care of a patient with clinical gas gangrene. We have previously pointed out that surgical amputation should be dictated by the vascular bed and not by the infection. The experiments as designed merely measure the virulence of the infecting organisms against the effectiveness of the prophylactic or therapeutic agent or agents and the resistance of the infected host. The evaluation of the various factors involved was simplified by the establishment of experimental conditions which would result in no impairment of circulation at the primary site of infection other than that produced by the disease itself. There was no complicating anesthesia.

#### SUMMARY

It has been possible to reproduce repeatedly in a large number of dogs experimental clostridial infections which in many respects are remarkably similar to clinical gas gangrene as it occurs in man. The main points of difference are in the mode

of production and the progress of the disease, which is much more rapid in the dog. Prophylactically, sulfadiazine was found to be the most effective sulfonamide employed, though it was valueless against *Cl. oedematiens*. Therapeutically, sulfadiazine was far from being routinely effective.

Penicillin, therapeutically, in massive doses early in the course of the disease gave excellent percentage survivals. It had no antitoxic properties and, when administered in small doses or late in the development of the disease, was not very effective.

Polyvalent antitoxin (Lederle) in massive doses administered rapidly (within a period of six hours) was effective even when administration was begun as late as twelve hours post-inoculation. Smaller doses given over a longer administration period were relatively ineffective. Massive doses did not routinely prevent varying degrees of local sepsis. A combination of polyvalent antitoxin and penicillin gave the best results when both per cent of survivals and reduced local sepsis were the criteria. Histologic examinations of the heart muscle in the control and treated animals would indicate that it is vital to institute adequate antitoxin therapy early in the course of the disease in order to reduce residual cardiac damage to a minimum.

*Cl. welchii* toxoid immunization was successful in protecting dogs against a pure strain inoculum of *Cl. welchii*. The degree of protection thus afforded was comparable to the results obtained following polyvalent antitoxin therapy. The critical alpha antitoxin titre was adjudged to be 0.1 unit per ml. of blood.

An interesting relationship was observed between diet in dogs and the capacity to produce adequate protective antitoxin titres.

NOTE: The work discussed in this paper was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the University of Rochester School of Medicine and Dentistry.

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<sup>4</sup> Dr. Milan A. Logan (personal communication).



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## DISCUSSION

**Robert P. Barden, M.D.** (Philadelphia, Penna.): When one considers the magnitude and fundamental importance of this six-year experimental study, it is easy to understand how inadequate I feel in attempting to discuss it. The only thing I can do is to compare some of Dr. Dowdy's results with clinical material reported in the litera-

ture based on battle experience. Most of what I have to say comes from an article by Langley and Winkelstein to which reference was made.

Dr. Dowdy has indicated that the clinical conditions in which gas bacillus infection occurs in man are somewhat different from the experimental conditions under which he studied it and therefore he would be the first to agree that the therapy may be altered by the altered clinical state. He mentioned the role of the vascular system, the vascular supply. In a battle casualty the status of the circulation is the most fundamental portion of the evaluation as far as treatment goes. He did not, of course, attempt to evaluate that in his animals.

The paper I refer to is based upon 96 proved gas bacillus infections in an Evacuation Hospital in Europe. The authors' experience seemed to indicate that in these soldiers prophylactic measures—chemotherapy—were not particularly useful and it was concluded that the most important single factor in prophylaxis was the initial cleansing of the wound by the first-aid man and the immediate bandaging and sanitary care which the wound received.

As far as therapeutic aspects go, it was found that sulfa drugs were useful in combating the secondary invaders, that penicillin was useful in large amounts because of its bacteriostatic action, and that antitoxin, as Dr. Dowdy indicated, was extremely important in selectively blocking the effects of the toxin produced by the organisms, particularly the late effects on the heart and distant structures, so that by no means am I saying that chemical agents should be abandoned.

I believe, however, that in human material one must not rely entirely upon medical treatment but be guided by the experience of the surgeons who felt that adequate and early surgery was the most single important factor. Of course, the delay period in battle casualties is very important and the difference between treatment instituted three days after the wound and six days after the wound is tremendous. In the first instance, the deaths ran around 11 per cent and in the second instance as high as 50 per cent.

Being a radiologist, I should say something, I suppose, about what this means in regard to radiation therapy. I am pretty well convinced that roentgen therapy is probably of no value and certainly should not be used in preference to any of these other measures that have been described. If one does use roentgen therapy at all, I think it extremely important to use it in multiple small doses, with an attempt, as with chemotherapy, to maintain a constant level: in other words, treatment every three, four, possibly six hours by the clock. Otherwise, we might just as well not try to talk about it.

Dr. Dowdy indicated that he had no explanation for the antagonism between sulfa drugs in

general and radiation therapy. I don't know whether he has any theoretical explanation or not, but the question is one that we are constantly asked by referring physicians.

**J. F. Kelly, M.D.** (Omaha, Nebr.): I cannot agree with the essayist when he says that he doesn't think there is anything to the x-ray treatment of gas gangrene. Nor can I see why we should spend time on experimental studies as to the effects of x-rays when their value is so clearly proved clinically and when reports from so many sources are available in the literature. It is fifteen years since I first registered my opinion on this subject and it has been confirmed by my own experience and that of many others in the ensuing interval. I should like to show some pictures of a young patient who was injured on a Sunday morning. In spite of continued administration of penicillin, gas gangrene developed and the patient was comatose when I first saw her the following Thursday. I instituted x-ray therapy at once, and by the next Sunday the patient was out of coma and recovery eventually ensued. [A series of slides illustrated Dr. Kelly's remarks.]

**Dr. Dowdy** (*closing*): In attempting to answer Dr. Barden's question, I am unable to say why there is this incompatibility, but I believe that it exists, and our experimental results would tend to verify this. Dr. Kelly has previously called our attention to this incompatibility of x-ray therapy and the sulfonamides.

With reference to Dr. Kelly's remarks, I am well aware of the work which he has done. In

fact, my first stimulation in regard to this disease resulted from the papers which he published some ten to twelve years ago when I was still with Dr. Doub in Detroit. This interest I carried with me to Rochester.

Some years ago we spent a considerable portion of our time looking for clinical cases of gas gangrene. It was customary for practically every case to receive roentgen therapy. In later years, however, we have recommended other types of treatment. In so doing, I believe we are correct.

In a recent paper, Dr. Kelly has emphasized the fact that x-rays require several hours to take effect. With this we are in agreement. We have pointed out experimentally in our dogs that one of the most severe damages is to the myocardium. One of my associates, Dr. Sewell, reported a case of gas gangrene which we had previously treated; this patient showed residual cardiac damage presumably resulting from his gas gangrene infection. Personally, if I had this disease, I would wish to be treated with large amounts of antitoxin plus penicillin. The earlier the antitoxin is given, in our opinion, the less likely is one to suffer chronic myocardial damage.

X-ray therapy is extremely beneficial in certain types of infection. We advocate it for post-partum mastitis, and at one time used it for the clinical treatment of gas gangrene. Experimentally with less severe infections, we have indicated that x-ray therapy is of some value. Even here it is not as efficacious as some of the other methods employed. In the future, it would seem that active human immunization will be possible, based on the work of Dr. Logan.



# A Study of Quality and Origin of Parasitic Radiation from the Target of an X-Ray Tube<sup>1</sup>

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WHEN AN IMAGE of the anode of an x-ray tube is obtained on a film placed before a lead diaphragm having an opening 1 mm. in diameter, all parts of the anode are reproduced, as shown in Fig. 1, thus indicating that they all emit x-rays. In the figure, zone A corresponds to that part of the tungsten target which receives the greatest bombardment of electrons; zone B represents the remainder of the tungsten target, and zone C the copper support,

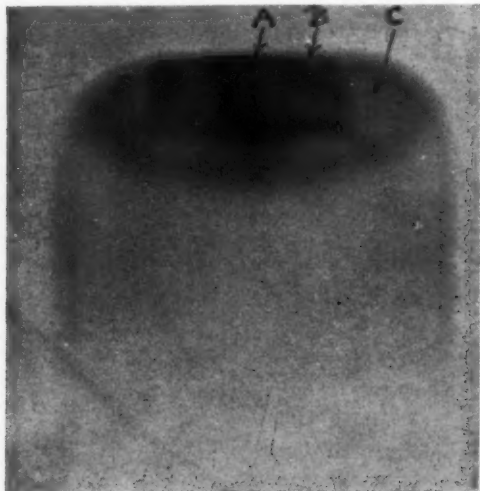


Fig. 1. Image of the anode, obtained through a diaphragm having an opening 1 mm. in diameter. Zone A corresponds to the part of the target receiving the greatest bombardment of electrons, zone B to the remainder of the tungsten target, and zone C to the copper support.

or anode stem. The intensity and quality of the radiation emitted by each of these zones have been studied by three methods: (1) independent micro-ionization chambers; (2) the Strauss dosimeter; (3) blackening of an x-ray film.

<sup>1</sup> Presented before the Société de Radiologie de Paris, May 12, 1946, and the Société de Electriciens, May 16, 1946. Published in *Rev. de radiol.* and in *Bull. de la Soc. d'électriciens*. Accepted for publication in *Radiology* in September 1946.

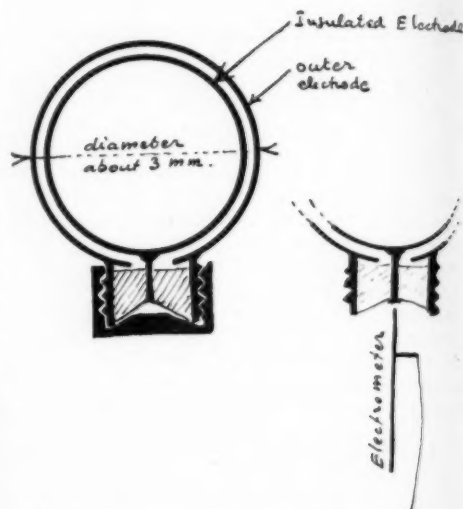


Fig. 2. One type of independent ionization chamber used in the studies recorded here. Larger chambers on the same principle, but of different form, are adapted for therapy and for measurement of scattered radiation received by the workers.

(1) For the purposes of this study an ionization chamber measuring but a few millimeters in diameter was constructed. For the central insulated electrode and the outer electrode a substance of low atomic weight, as magnesium or some organic product, was used. The charge of the central electrode and the charge remaining after exposure are measured by means of a special electrometer providing an automatic charge, called by us "radiometre."

(2) The Strauss dosimeter measurements were made in accordance with the usual technic.

(3) The third method consisted in comparing the degree of blackening of an x-ray film with the aid of a densitometer, a standard scale of tints being used for quantitative determinations.

With the micro-ionization chambers, it was found that at 100 kv. the greater the diameter of the aperture in the lead diaphragm, the more penetrating was the radiation. This observation prompted us to investigate the influence of the different parts of the anode upon the quality of the

the radiation from the different zones, when the distance between the anode and the ionization chamber was 16 inches, was found to be as follows:

- Zone A.....1.75 mm. aluminum.  
 Zone B.....2.30 mm. aluminum.  
 Zone C.....2.35 mm. aluminum.

The intensity of the radiation from zone A was 220 times that from B, while the intensity of the radiation from B was twice that from C. It does not follow, however, that zone B is responsible for only 1/220 and zone C for only 1/440 of the total radiation, since zones B and C are much larger than A. It is conceivable, therefore, that they may exert a notable influence on the quality of the radiation from any given tube.

When the limiting diaphragm used for the preceding study was withdrawn, the half-value layer at the same distance, *i.e.*, 16 inches, was found to be 2.0 mm.

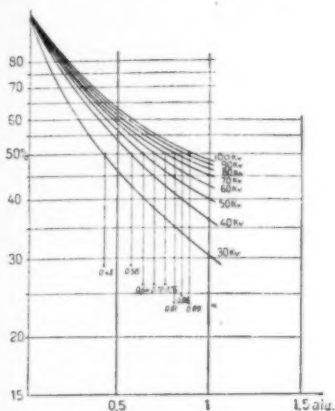


Fig. 3. Curves showing absorption of the radiation (total) in aluminum at voltages of 30 to 100 kv. at 30 cm. distance from the anode. Ordinates: Percentage of transmitted radiation. Abscissas: Filtration in millimeters of aluminum.

radiation. For this purpose the pin-hole diaphragm used to obtain the image of the anode was employed, the ionization chambers being placed successively in each of the three zones, A, B, and C. As will be explained more fully below, it was found that the radiation emitted by the central zone, A, was of the greatest wave length, while the most penetrating rays were those from zones B and C. These results were confirmed by densitometer determinations. The experiment was completed by a study of the effect of distance upon the quality of the radiation. It was found that with a large aperture in the limiting diaphragm, the radiation was most penetrating at the point of exit of the tube.

#### DETAILS OF EXPERIMENTAL STUDIES

(1) *Determinations with Micro-Ionization Chambers:* With the specially constructed ionization chambers, the half-value layer of

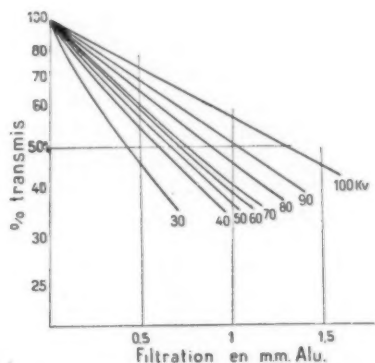


Fig. 4. Curves showing absorption of the radiation (total) in aluminum at voltages from 30 to 100 kv. at 8 cm. distance from the anode. Ordinates: Percentage of transmitted radiation. Abscissas: Filtration in millimeters of aluminum.

aluminum. This figure falls within the penetration range of zones A, B, and C. It represents, in fact, the total radiation from all three zones.

The difference between the quality of the radiation emitted by the central zone only and the total output was determined also for other distances. At 3

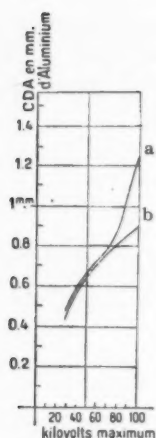


Fig. 5. Variations in half-value-layer as a function of the maximum voltage applied to the tube, at distances of 8 cm. (a) and 30 cm. (b). The curves are practically identical up to 70 kv. but diverge sharply as the voltage is increased above that point.

inches from the target the half-value layer for a narrow beam of rays, issuing only from zone A, was shown to be 1.80 mm. aluminum, but the half-value layer of the broad beam, representing all three zones, was 2.25 mm. aluminum.

It is thus apparent that for the narrow beams, representing radiation from zone A alone, the quality is practically the same at 3 inches (h.v.l. 1.80 mm. Al) and at 16 inches (1.75 mm. Al). For the broad beam, however, obtained without the diaphragm, there is a notable difference (2.25 mm. Al at 3 inches, 2 mm. Al at 16 inches).

Before attempting to interpret these observations, the results obtained with the other methods of study may be set forth.

(2) *Determinations with the Strauss Dosimeter:* In this study the dimensions of the ionization chamber, which measures about 1 inch, precluded observations on narrow beams, and all measurements apply therefore to broad beams, without a limiting diaphragm. Figures 3 and 4 show the absorption in aluminum at 16 and at 3 inches, while Figure 5 shows the half-value layer in relation to voltage. It is seen in this last figure that for low volt-

ages the penetration at distances of 16 and 3 inches is the same, but at voltages above 70 kv. the curves separate, the half-value layer at 3 inches (1.25 mm. Al) being notably higher than at 16 inches (0.9 mm. Al).

It will be noticed that at both distances the half-value layer as determined by the Strauss dosimeter is lower than that obtained with the micro-ionization chamber. This is to be explained by the fact that the specially constructed microchambers had an outer electrode of aluminum. Because of this, the less penetrating rays were

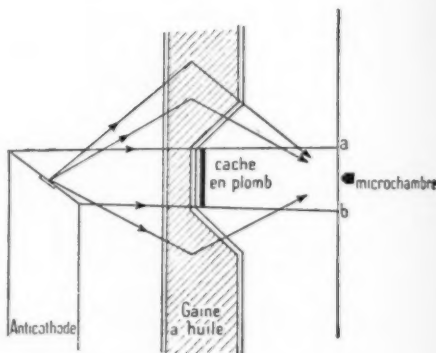


Fig. 6. Measurement of scattered radiation, with the tube exit covered with 3 cm. of lead and a thin sheet of aluminum.

eliminated and a much higher half-value layer was obtained.

(3) *Blackening of an X-Ray Film:* By this method the half-value layer at 16 inches for 100-kv. radiation with the limiting diaphragm was found to be as follows:

Zone A.....	1.10 mm. Al
Zone B.....	1.50 mm. Al
Zone C.....	1.70 mm. Al

On withdrawal of the diaphragm we should expect, as with the micro-ionization chambers, to obtain a half-value layer within this range (1.10-1.70 mm. Al). The figure actually, however, was 1.0 mm. Al. This indicates that, when the diaphragm is withdrawn, there is added to the total output of the anode a very soft radiation scattered by the sides of the tube.



When ionization chambers are used for the measurements, this scattered radiation is largely eliminated by the walls of the chamber so that there is no lowering of the half-value layer of the total radiation.

In order to study this scattered radiation, a film was placed 3 inches from the anode, the central opening of the tube was covered by a sheet of lead 3 mm. thick and over this was placed a thin sheet of aluminum to eliminate the radiation scat-

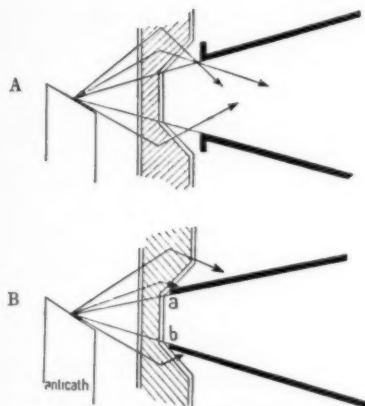


Fig. 7. Effect of a localizing cone on the scattered radiation. This is eliminated only if the cone is in direct contact with the tube, as in B. When the cone is placed at a distance from the tube, as in A, the greater part of the scattered rays are transmitted.

tered by the lead. With this arrangement, the radiation coming directly from the anode is suppressed completely for one part of the film, but the entire film receives the radiation scattered by the sides of the tube. This is shown in Figure 6, in which the area between *a* and *b* receives only the scattered rays. The half-value layer of this scattered radiation was found to be 0.5 mm. Al.

The only way in which this scattered radiation may be eliminated is by placing a localizing cone directly against the tube, as in Fig. 7 B. A similar cone at a greater distance, as in Fig. 7 A, will be ineffective, as it will permit the passage of the greater part of the scattered rays.

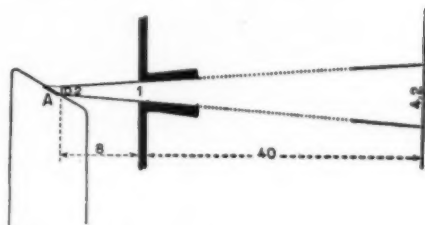


Fig. 8. Showing the decrease in the field with reduction of the aperture in the cone. At 40 cm., for a 10 mm. opening the field receiving the total radiation from zone A measures only 4.2 cm.

The question arises whether a cone with a small opening might not be used to eliminate radiation issuing from zones B and C, allowing only the radiation from zone A to pass. As is shown by Figure 8, however, the aperture of the cone cannot be reduced

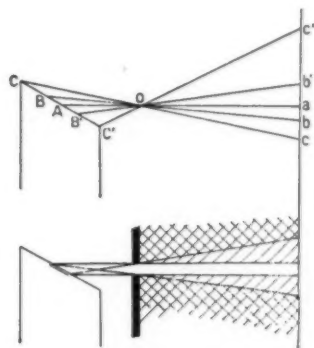


Fig. 9. Series of images of a given point, O, due to the radiation from the three zones.

without an altogether disproportionate reduction of the area of projection. Thus for a cone 1 cm. in diameter in contact with the tube, the area of projection at a distance of 16 inches is less than 2 inches in diameter, considering, that is, the area of the film receiving radiation from the entire zone A.

The area of projection required for fluoroscopy and roentgenography demands a cone of such size that only a small fraction of the parasitic radiation from zones B and C is eliminated. As a result of this radiation, a series of shadows of any pro-

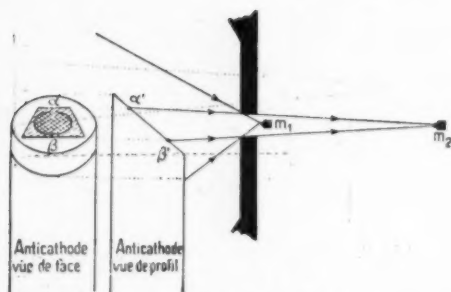


Fig. 10. Diagram illustrating the quality of radiation at the point of opening of the tube ( $m_1$ ) and at a distance ( $m_2$ ).

jected point is produced, which results in diffusion of detail and consequent lack of definition in the image. This is shown in Figure 9, where 0 is the given point,  $a$  is the principal image, and  $b$ ,  $c$ ,  $b^1$  and  $c^1$  are the images due to the radiation from zones B and C. Since we cannot eliminate this parasitic radiation from the anode stem, we must reduce the metal volume of the latter as much as possible. The rotating anode has this advantage along with others.

#### DISCUSSION

It has been shown by the use of a diaphragm that the radiation emitted by zones B and C (Fig. 1) is more penetrating than that from zone A. Without a diaphragm the radiation is most penetrating just against the exit of the tube. This may be explained by reference to Fig. 10. In the figure, microchamber  $m_1$  is placed just against the opening of the tube, where it receives radiation from almost all parts of the target and the anode stem. Microchamber  $m_2$ , on the other hand, at a distance from the tube, receives chiefly radiation from zone A, without the more penetrating rays from zones B and C.

It remains to explain the greater penetration of the radiation from those parts of the anode at a distance from the principal focus, A, that is from zones B and C,

and the increase in penetration as this distance is increased. Electrons emitted by the cathode assume, as a result of the difference of potential between the filament and the anode, a kinetic energy which is a function of the difference in potential. The penetration of the radiation emitted by different parts of the anode bombarded by these electrons is, in turn, a function of their kinetic energy. It may be concluded, then, that the electrons striking zones B and C have a greater velocity than those reaching zone A, since the distance which they must travel to reach the point of impact is greater.

This fact can be explained by the repelling force (space charge effect) exerted by the electrons which reach zone A in high concentration, upon the electrons following behind them. Because of this, the sum total of electrons bombarding zone A have a lower velocity than would be expected if only the voltage applied to the tube were taken into consideration. Electrons bombarding B and C are not subject to this repelling force and therefore, falling upon these zones with their full velocity, produce a more penetrating radiation.

As noted as early as 1916 in a study of the early Coolidge tubes, given a constant voltage, the radiation becomes less penetrating as the intensity and, correspondingly, the concentration of electrons bombarding the anode are increased. It should be further noted that the degree of penetration increases with the distance of the source from the center of the tungsten target.

These phenomena have a significance for both radiography and radiotherapy that cannot be neglected.

NOTE: This study was made in Paris at the Laboratoire de Radiobiologie du Centre Anticancereux de l'Hôpital Tenon, with a Picker X-ray Generator of the type used by the U. S. Army.

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# Chronic Salmonella Bone Infection<sup>1</sup>

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IT IS NOW GENERALLY recognized that systemic infection with organisms of the Salmonella group is not of rare occurrence. The literature abounds with reports of cases involving almost every system of the body. Most of the reported cases have been of the acute toxic type with severe constitutional reactions, and the patients have been chiefly infants and children. Few if any of the cases reported deal with the chronic form of the disease, *i.e.*, a localized pyogenic infection.

Recently we encountered an unusual example of chronic bone infection involving the lower end of the tibia which proved to be of the Salmonella type.

## CASE REPORT

S. S., male, age 20, was referred for x-ray examination of the left ankle region. In 1940, while playing ball, he had twisted his ankle and it became painful and swollen. After a short course of baking and diathermy by his family physician the ankle became normal. Some six months later a similar episode occurred after slight activity, and this was repeated from time to time. In 1942, x-ray studies revealed a cystic degenerative process involving the metaphyseal portion of the tibia and extending into the internal malleolus. In spite of this, the patient was inducted into the Armed Forces in 1943. While he was undergoing basic training, the ankle suddenly became swollen and a cellulitis developed, requiring incision and drainage. After several weeks the lesion healed, and shortly afterward the patient was given a medical discharge. In April of 1945, while he was at college, pain and swelling of the ankle again occurred spontaneously. He returned to his home and x-ray studies again revealed cystic changes in the lower tibia.

The patient gave no history of any past acute infection, food poisoning, typhoid fever, or paratyphoid infection. Aside from a mild form of "swollen glands" in childhood, he had always been perfectly well.

A physical examination was negative, except for the local findings. There were moderate soft-tissue swelling and redness about the ankle region, with an old scar over the medial aspect of the ankle, the re-

sult of previous incision and drainage. Motion of the ankle was partially restricted in all directions and there was marked tenderness over the anterior and medial aspect of the lower end of the tibia.

X-ray examination revealed several irregular areas of cystic change in the lower end of the tibia extending into the internal malleolus. The larger cystic area was oval in shape, fairly well defined, presenting some reactive changes in the walls. The smaller absorptive areas were less clearly defined and showed only slight reactive changes. There was no expansion of the shaft, and the cortices appeared intact. The ankle joint was preserved. The impression was that of multiple small bone abscesses.

*Differential Diagnosis:* Giant-cell tumor was considered in the differential diagnosis because of the location of the lesion in the metaphyseal and epiphyseal end of the tibia. The absence of trabeculation, together with the reactive process about the absorptive areas, tended to exclude this possibility. A tuberculous process was also considered and was difficult to exclude. The absence of demineralization and an intact joint militated against that diagnosis. A fibroma may present an appearance similar to that observed, but there is usually a single localized area of involvement with no particular reactive changes. Also, fibromata are not apt to be located in metaphyseal areas.

*Operative Findings:* A 3-inch incision was made over the anteromedial aspect of the right tibia. The periosteum showed some thickening. On removing the cortex at a depth of about 1/2 inch, a caseous mass of tissue was encountered measuring approximately 3/4 inch. This was located about 2 inches above the internal malleolus. On continuing the bone dissection into the malleolus, three additional foci were opened up. The last of these was located near the ankle joint and contained three or four drops of fluid pus. At one point the lesion extended so close to the joint space that a small bit of cartilage of the joint was removed in opening up the focus. This cartilage measured about 1/8 inch in diameter. A smear and culture were taken and a specimen of tissue was removed for microscopic examination. The wound was closed in the usual manner, and a cast was applied.

*Gross Pathology:* The specimen consisted of many fragments of spongy bone and some of cortical bone. Among the bits of tissue, one could find pieces of inflammatory membrane, some of which were free and some adherent to the spongy bone. Some of the spongy bone showed cavities containing whitish, almost chalk-colored, pus.

<sup>1</sup> Accepted for publication in September 1946.



Fig. 1. Localized cystic changes in the lower end of the tibia.

**Microscopic Study:** Sections showed evidence of chronic osteomyelitis of a rather nondescript histologic nature. Some fields were heavily permeated with polymorphonuclear leukocytes and interspersed with macrophages, some of which were filled with lipid. In other fields, the inflammatory cells in the marrow spaces were essentially lymphocytes and macrophages.

The diagnosis was chronic bone abscess. *Salmonella Oranienburg* was obtained on culture.

According to Seligmann and Saphra, about 38 different types of *Salmonella* have been identified. Some have been found rather infrequently, others seldom, a few only in a single instance. The predominant type is *Salmonella typhi murium* of group B, which occurs in 3 per cent of the cases studied. Next in frequency are members of group C—*S. Newport*, *S. cholerae suis*, *S. Oranienburg*, *S. Montevideo*, and *S. paratyphi B*. Forty-nine per cent of the *Salmonella* infections belong to group B, 33 per cent to group C, 6 per cent

to group D, and 6 per cent to group E. The other groups together account for 4.1 per cent.

In recent years the steady progress in the differentiation of the various types of *Salmonella* organisms and constant improvement in the methods of differentiation have broadened our knowledge and consequently our diagnostic acumen in this particular group of infections. Most of the cases are diagnosed by agglutination reactions with stock serum and proved by various culture methods. The National *Salmonella* Center, New York City, headed by Dr. Erich Seligmann, has done much to enhance our knowledge of the bacteriology and epidemiology of this group of organisms.

*Salmonella Oranienburg* is one of the paratyphoid group of organisms. The members of this group resemble each other closely, being gram-negative motile rods.



Fig. 2. Cystic changes in the lower end of the tibia with extension into the internal malleolus.

Differentiation by morphological cultural and sometimes even sugar fermentation methods is impossible. Agglutination by specific antisera and agglutination absorption are required for final differentiation.

*Salmonella Oranienburg* has been found in animals and human beings. It has the typical characteristics of *Salmonella* cultures in so far as it does not produce indol. It ferments under gas production, dextrose, maltose, and manitol. Furthermore, of the rarer sugars, it attacks arabinose, dulcitol, rhamnose, trehalose, xylose, but not inositol. It is able to utilize the different tartrates and citrates.

#### SUMMARY

A case is presented of chronic multiple bone abscesses of the lower end of the tibia which proved to be due to *Salmonella*. It is important to bear this organism in mind when dealing with chronic pyogenic infections of bone.

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# Calcification of Pleura and Lung<sup>1</sup>

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**C**ALCIFICATION of the pleura or of the lung is not uncommon, but the massive involvement of an entire lung is so rare that the following case may be of interest. A few such lesions have been reported in the American and foreign literature, but none of these has been studied by body-section (planigraphic) roentgenography.

## CASE REPORT

A white female of 74 years gave a history of diphtheria and scarlet fever in youth, pneumonia at 40 years, influenza at 42 years, and pulmonary tuberculosis with pleuritis (hospitalization for one year) also at 42 years. The diagnosis of tuberculosis was confirmed by two sputum samples of separate date positive for acid-fast bacilli. Symptoms at that time (1912) included cough, fever, and left thoracic pain. No thoracentesis or roentgen study was done.

There were two admissions to the Hospital of the University of Pennsylvania, in 1915 and 1924, because of pain in the left shoulder, thorax, and lumbar area, loss of weight, hoarseness, dyspnea, palpitation, and vertigo. At these times expansion was almost entirely right thoracic; tactile fremitus and vocal resonance were increased on the left above the 7th rib posteriorly. There were bronchial breath sounds, whispered pectoriloquy, depression of the supraclavicular fossa, and dullness to percussion on the left. The heart and trachea were constantly retracted to the left. On the second admission, the sputum was negative for acid-fast bacilli and roentgen study of the chest revealed no expansion on the left, the heart retracted to the left lateral chest wall, and left deviation of the trachea. Other findings were probable thickening of the pleura and pulmonary fibrosis, and a suggestion of encroachment by emphysematous right lung upon the left hemithorax. (The plates were not available for review.) No mention was made of calcification.

From 1934 to 1945 the patient has been seen by Dr. O. H. Perry Pepper (to whom we are indebted for this report), as an outpatient. She has been in rather good health, suffering occasionally and moderately from cough, weakness, dyspnea, vertigo, sore chest or shoulder, and "heart attacks." However, these do not prevent her doing all her housework and driving a car.

## DISCUSSION

High-speed Potter-Bucky roentgenograms in the postero-anterior and lateral projections reveal an extensive calcification in the left thorax and obscuration of the heart (Fig. 2, A and B). The contour of the upper and lower lobes can be seen well, and apparently both have undergone contraction with upward displacement. The right lung has expanded across the mid-line. The distance between the left rib cage and the calcium might be due to an uncalcified parietal pleura, but may be attributable simply to the fact that the shrunken lung lies posteriorly in the thorax and does not reach the lateral wall at its greatest diameter. This is analogous to a plan view of a spherical jar partly occupied by an opaque material (as in the accompanying sketch, Fig. 3).

Spiral laminagraphic exposures done in the anteroposterior and lateral projections reveal a diffuse homogeneous density throughout the left lung, and splotchy, granular calcium placed irregularly (Figs. 4-13).

There has been a great deal of discussion in our clinic and among other roentgenologists and phthisiologists to whom we have shown these films. One group holds that the lesion is a calcification chiefly of the lung and also of the pleura, while the other maintains that this is principally a pleural calcification, with perhaps some small calcific lesions in the lung. Both agree fairly well that the lung has been the seat of severe contraction.

The theory that this is chiefly a lung lesion but also a pleural one is supported by the homogeneous density best seen in the planigraphic studies (Figs. 5, 6, 7, 11, 12, 13). Furthermore, the persistence

<sup>1</sup> From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Penna. Accepted for publication in September 1946.

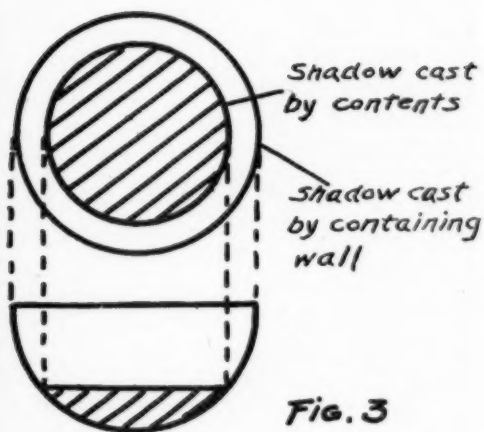
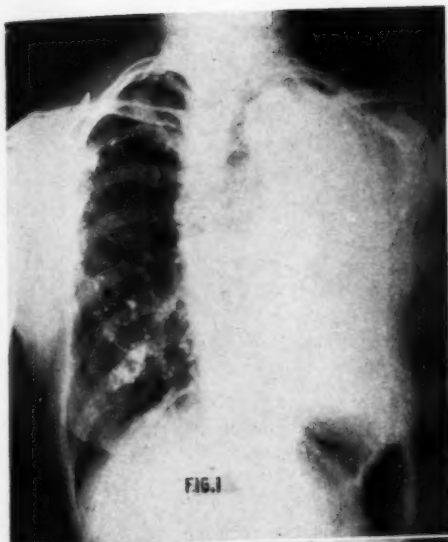
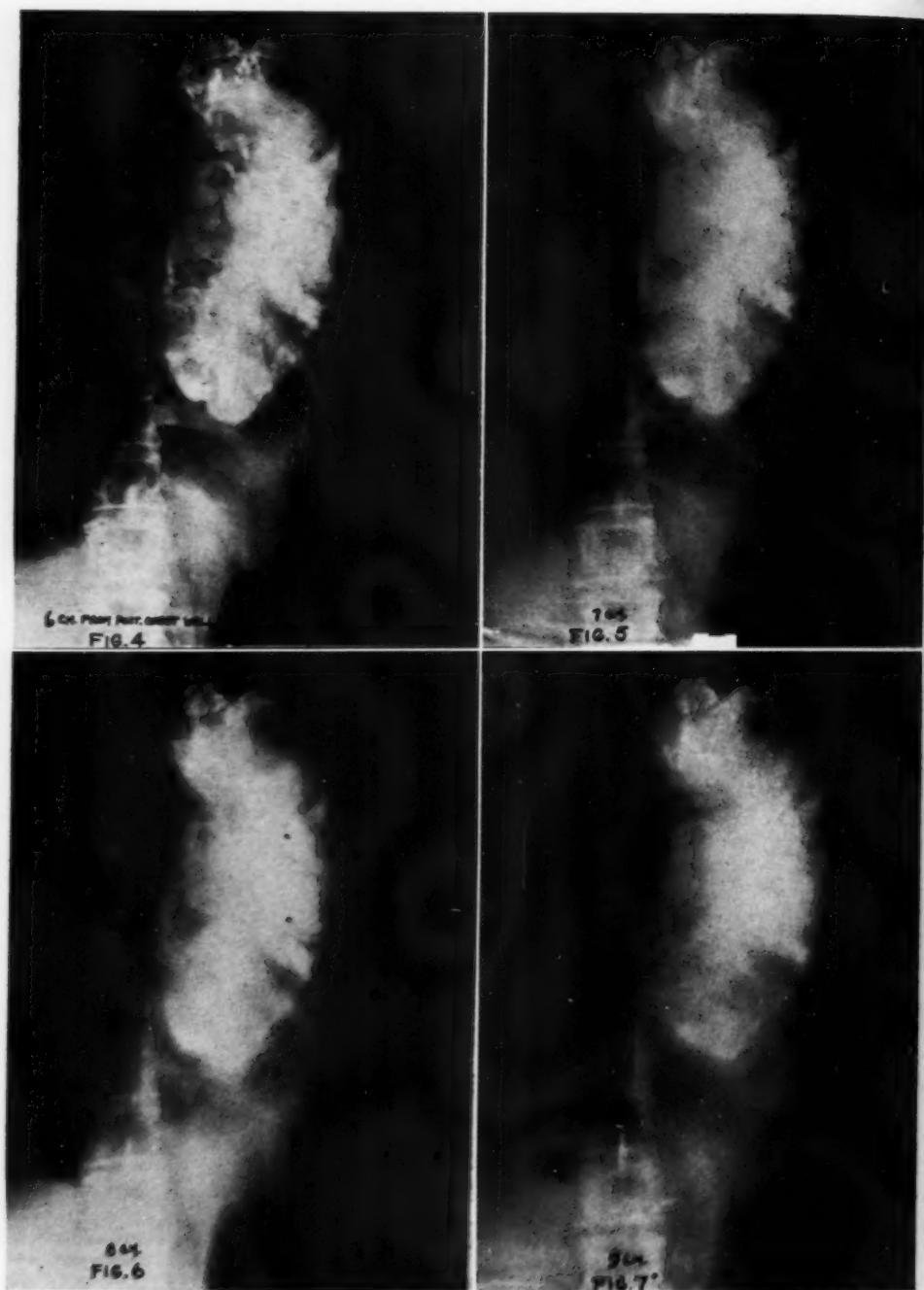


Fig. 1. Standard non-Bucky film.

Fig. 2, A and B. Bucky postero-anterior and lateral films.

Fig. 3. Sketch of partly filled vessel.



Figs. 4-7. Planigraphic exposures, anteroposterior, of left side.



Figs. 8-10. Planigraphic exposures, anteroposterior, of left side.

in many sections of the sharply outlined, dense, granular opacities within the periphery of the organ lends greater conviction to this view. The right lung also contains many discrete areas of calcium that are regarded as healed parenchymal tuberculous foci and there are probably similar lesions in the left lung. In addition, these proponents believe that, were the disease limited to the pleura, the great degree of contraction of the lung and herniation of the right lung into the left side would not be present.

On the score of this being principally a pleural lesion it is said that a densely fibrosed contracted lung and a probably thick hyaline pleura (underlying the calcium) would, very readily, provide a large degree of the homogeneous density seen. The adherents of this view believe that the dense granular areas lie along the pleural borders of the left lung and likewise in the right lung; that the planigraphic sections slice straight across the curving, constantly changing course of the lobar borders (in-



Figs. 11-13. Planigraphic exposures, lateral projection.

cluding the interlobar pleura), where the dense patches may be seen located by the conventional Bucky films; and that this

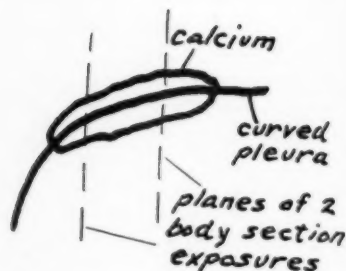


FIG. 14

Fig. 14. Two laminagrams on parallel planes may nearly duplicate each other and suggest location inside the lung.

phenomenon causes many densities to be seen rather well at slightly changed locations as one proceeds from one to another of the planigraphic sections (Figs. 4-13). If this pleural location is true, it will also cause the body sections to suggest or imitate a parenchymal location of the plaques of calcium (Figs. 14 and 15).

Although this is a proved case of pulmonary tuberculosis, no necropsy study



can be presented, as the patient is living. However, this report does serve to reveal some methods and theories used and some limitations encountered in attempting to diagnose thoracic lesions roentgenographically.

NOTE: Grateful acknowledgment is made to Dr. O. H. Perry Pepper for his permission to publish this case.

Jeanes Hospital  
Fox Chase, Philadelphia 11,  
Penna.

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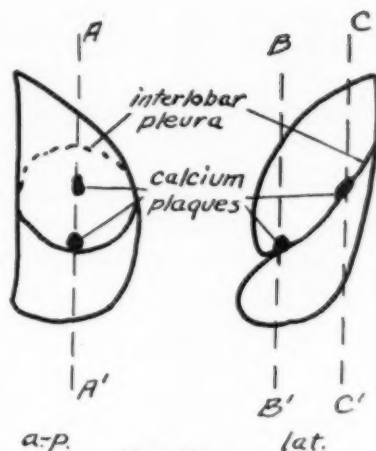


FIG. 15

Fig. 15. Sketch of anteroposterior and lateral projections to show how laminagraphic section A-A' will clarify two calcium bodies on the pleura, but how sections B-B' and C-C' will cause areas to lie apparently within the lung.

PRITCHARD, J. S.: Some Interesting Cases of Calcareous Degeneration Found in the Thorax. *Arch. Int. Med.* 32: 259-282, August 1923.



# EDITORIAL

## The Present Status of Cancer Research

During the past three or four decades a tremendous amount of information has been acquired regarding the carcinogenic process. Up to the present time, search for a single cause of cancer has been fruitless. The great majority of modern cancer investigators will agree that the cause of cancer, unlike that of the communicable diseases, is complex and multiple. Cancer can now be induced at will in experimental animals by (a) more than 200 different chemicals, some of which are organ specific and induce the process in one organ or tissue only; (b) many of the energy agents (x-rays, ultraviolet light, gamma rays, etc.), especially when the tissues are subjected to interval exposures; (c) hormonal disturbances and imbalances; (d) genetic manipulations (inbreeding and cross-breeding); (e) a combination of one or more of the above factors. Recently, Copeland and Salmon<sup>1</sup> of the Alabama Polytechnic Institute have reported the induction of cancer in rats by means of a simple dietary (choline) deficiency.

While much has been learned about the inciting causes of cancer, which the late Dr. James Ewing called the "causal genesis," little or nothing has been discovered concerning Ewing's "formal genesis," or the intracellular changes that take place when normal cells are transformed into cancer cells. Some think this transformation is the same for all cancers. On the other hand, this mechanism, too, may be complex and multiple, and many theories have been advanced as to its nature. But regardless of whether the intracellular change is due to a somatic mutation, to an intracellular parasitic virus, to modified mitochondria as suggested by duBuy and

Woods<sup>2</sup>, to a retrograde bacterium-virus which has "hybridized" the cell, as suggested by Robert Green<sup>3</sup>, or to an altered protein enzyme as set forth by Potter<sup>4</sup>, the final result in every case is the same. We observe a deviation from the normal cell behavior-pattern in which cells contribute nothing to the organism as a whole but live at its expense and thrive while the rest of the body is wasting away. This is the concept regarding the nature of the cancer process toward which modern research has lead us. If it is correct, cancer may be thought of as an "autoparasite," or better perhaps an "autosite" (Gr. *αὐτός*, self + *σῆμα* food) The latter term has been used in the past to designate a monster capable of an independent existence after birth or a member of a double fetal monstrosity that nourishes itself by its own organs and, also, by nourishment from the other member. There is a good reason to believe that some cancers, especially those of early childhood, differ from these monstrosities in degree more than in kind. While monstrosities invariably develop during intra-uterine life and are apparent at birth, the abnormal and equally monstrous growth we call cancer may occur at any time during the entire development (intra-uterine and post-natal) of the individual. Moreover, cancer, for reasons not yet clear, displays a tremendous jump in mortality after the age of 44. In 1940, the age specific death rate in the United States was 61.1 per 100,000 deaths for the age group 35 to 44, while it was 168.8 per 100,000 for the age group 45 to 54, and 1,183.4 for the age group 75 years and

<sup>2</sup> Science 102: 591, 1945.

<sup>3</sup> Biodynamica 6: 1-21, 1946.

<sup>4</sup> Cancer Res. 3: 358-361, 1943.

<sup>1</sup> Am. J. Path. 22: 1059-1079, 1946.

over<sup>6</sup>. "When the patient is over 40 think of cancer first" is a slogan that every conscientious physician will adopt when making a physical examination.

Progress in the therapy of cancer has been relatively slow. Radium, x-rays, and surgery remain our most effective weapons provided diagnosis is made early and the patient falls in expert hands. Since World War II cancer research has been greatly accelerated in the United States. The American Cancer Society, upon the recommendations of the Committee on Growth of the National Research Council has allocated over \$1,500,000 to cancer investigations throughout the country, and the National Cancer Institute, upon the recommendations of the National Advisory Cancer Council, has distributed \$500,000 since July 1, 1946. Still larger sums from

both private and tax-supported sources will be available after July 1947. The emphasis today in cancer research is shifting from studies on the carcinogenic process toward chemotherapy. The recent advances made in our knowledge of the sex hormones in relation to the growth of certain types of cancer, the effect of nutrition (restricted caloric diet) on experimental animal cancers, both spontaneous and induced, and the discovery that certain chemicals seem to have selective effects on cancer cells have encouraged workers to concentrate upon the chemotherapeutic approach. No one can say, however, which approach is most promising, and the final solution may come from a totally unexpected source.

R. R. SPENCER, M.D.

*Chief of the National Cancer Institute  
Bethesda, Md.*

<sup>6</sup> Illinois Cancer Bull. 1: 3, April 1946.

## Annual Meeting Radiological Society of North America

The Thirty-third Annual Meeting of the Radiological Society of North America will be held in Boston, with headquarters at the Hotel Statler, from November 30 to December 5, 1947.

## ANNOUNCEMENTS AND BOOK REVIEWS

### GEORGIA RADIOLOGICAL SOCIETY

At the recent meeting of the Georgia Radiological Society, held in conjunction with the Medical Association of Georgia, Dr. Albert Rayle of Atlanta was elected president, Dr. Harry McGee of Savannah vice-president, and Dr. Robert Drane of Savannah secretary-treasurer.

Dr. Clarence Allen Goode, Jr., of the Mayo Clinic spoke on "The Roentgenologic Diagnosis of Tumors of the Small Intestine." Papers were also presented by Drs. L. P. Holmes, Stephen W. Brown, and David Robinson from the University School of Medicine, Augusta; Dr. James J. Clark of Atlanta; Dr. H. H. McGee of Savannah; Dr. Max Mass of Macon; and Dr. R. C. Pendergrass of Americus.

Arrangements were made to hold the mid-winter meeting of the Society at Tybee Beach.

### PROFESSOR H. HOLTHUSEN

In the December (1946) issue of *RADIOLOGY* we were pleased to reprint some excerpts from a letter from Professor Holthusen of Hamburg, Germany. In a more recent letter, addressed to Dr. George Pfahler, Dr. Holthusen, acknowledging receipt of a "Care" package writes:

"While we are approaching the middle of March, we are still in hard winter. The snow lies higher than anybody can remember, the ice on the Elbe above Hamburg has more than one meter. From the coast you can drive in a motor car to the islands, a fact that never has been realized as long as historical tradition exists. Since the middle of January the temperature only on two days in the past week has risen above zero. Fuel could not be delivered to the population and at the time being cannot even be transported to the electric power stations, so that in the evening, we generally sit in the dark. You can imagine what a value the supplementary calories of your gift represent in these extraordinary times as a compensation for the loss of warmth. But I confess they are the more welcome to us as we regard them as a token of your undiminished friendship to us. . . .

"We have passed these hard weeks in a comparatively good position, as we had warm room at home and as the hospital was comparatively well heated. It is only since the beginning of March that the supply of fuel has come to an end. . . .

"Not long ago we celebrated the 80th birthday of Prof. Walter. You remember perhaps his co-operation with Albers-Schönberg in the field of Röntgen-technique. He was a physicist and invented the water-cooled tube. He is still quite up to date and is to be found at his bureau at the Physical Institute nearly every day. Soon we are relying entirely upon the 'second generation.'"



Professor Adolf Liechti

### In Memoriam

PROFESSOR ADOLF LIECHTI

1898-1946

In the death, in August 1946, of Professor Liechti, head of the Central Radiological Institute of Bern University, the whole medical world has suffered a great loss, as have all who had the privilege of knowing personally this modest, kindly man. Because of the illness which he bore with such admirable courage, his appearance abroad was infrequent, but his pioneer work in every branch of radiology was known far and wide.

Under the direction of Hermann Holthusen, the leading German radiologist of the time, there appeared in 1929 Liechti's standard treatise on the measurement of the quality and quantity of roentgen rays, a work which is still considered as the most important foundation of radiotherapy. Liechti's particular bent for physics was also seen in his creation of an entirely new type of combined electrocardiograph and x-ray apparatus, which makes possible specifically focused roentgenograms of the heart at any phase of cardiac activity, and in his

textbook on roentgen physics, probably the most authoritative work on the subject.

But Liechti was in no sense interested in radiology solely as a branch of physics; he conducted radiobiological research with the same supreme ability which he brought to the solution of physical problems. It would be impossible to enumerate here even the more important of his works on radiobiology. The great services he rendered to medical radiology are no way less valuable. In the last stages of his illness he still carried on his work as a practising radiologist at several hospitals in Bern and his private institute, in addition to his university activities. All who had occasion to consult him were inspired with the deepest admiration of his personal qualities as well as his supreme knowledge of radiodiagnosis and radiotherapy. His last great work, *Radiodiagnosis of the Vertebral Column* (Springer, Vienna, 1944) was closely related to his own tragic affliction and, like all his works, is distinguished by a unique mastery of the subject.

Swiss radiology has indeed suffered an irreparable loss by the death of Professor Liechti. None will be able to fill his place. But all who knew and honored this unusual radiologist will feel themselves in duty bound to maintain his spiritual legacy, radiophysics, radiobiology and medical radiology, as equally important branches of radiology. Thus will the torch he set alight be carried forward. O. HUBACHER

Bern, Switzerland

#### RICHARD MANGES SMITH

1901-1947

Richard Manges Smith was born in York, Penna., on Jan. 25, 1901, the son of George E. and Leah Jenny Manges Smith. He received his education at Gettysburg College and later attended Jefferson Medical College, receiving his degree from that institution in 1927, and serving his internship there. He then became associated with his uncle, Doctor Willis F. Manges, for the study of radiology and advanced rapidly in this specialty. He first held the position of Assistant Demonstrator in Roentgenology in the Jefferson Medical College and was later elevated to Instructor and Demonstrator.

Dr. Smith's career was tragically cut short by an illness which began in 1936 and was slowly progressive until his death on Nov. 20, 1946. His lingering illness was due to multiple sclerosis. Since 1939 he had been inactive in the Department of Roentgenology at Jefferson Hospital. In that year he married Marion E. Bowers, who faithfully cared for him until his death.

Doctor Smith's career, though short, led to his recognition by election to membership in the American College of Radiology, the American Roentgen Ray Society, the Radiological Society of North America, the Philadelphia Roentgen Ray Society, and the College of Physicians and Surgeons of Philadelphia. He was a member of Nu Sigma Nu and Sigma Alpha Epsilon fraternities.

Doctor Smith had made many friends during his work at Jefferson. His optimism in spite of his affliction, his great sense of humor, his accomplishments and friendliness all won him great admiration. His friends in radiology mourn his passing.

PAUL C. SWENSON, M.D.

## Book Reviews

**RADIOLOGY FOR MEDICAL STUDENTS.** By FRED JENNER HODGES, M.D., Professor and Chairman, Department of Roentgenology, University of Michigan, ISADORE LAMPE, M.D., Associate Professor, Department of Roentgenology, University of Michigan, and JOHN FLOYD HOLT, M.D., Assistant Professor, Department of Roentgenology, University of Michigan. A volume of 424 pages, with 103 plates. Published by The Year Book Publishers, Inc., 304 S. Dearborn St., Chicago 4, Ill. Price \$6.75.

The expansion in the teaching of radiology has brought with it the publication of a number of textbooks; the latest addition by the University of Michigan group is a splendid contribution. Designed especially for the undergraduate student, the book fulfills admirably the purpose of the authors to furnish a well balanced succinct presentation of the subject. The attempt has been made to cover to a limited degree x-ray technic, to a reasonably elaborate degree roentgen diagnosis, and perhaps to an even greater degree than is really necessary for the undergraduate student, radiation therapy. The general principles underlying x-ray technic are well presented, although the details are not elaborated upon. The manner of reporting films is described fully and the one detailed report is a most satisfactory example.

There are few criticisms to offer on this excellent book. The information contained is entirely accurate and is presented in systematic fashion. The text is well written, the choice of illustrations is good and the whole manner of presentation is highly satisfying. A moderate-sized, well selected bibliography is appended to each chapter. It would have been desirable to have included more detail on the specific indications for roentgen examination and on the evaluation of the results of x-ray examination in particular conditions. A serious omission is the absence of any discussion of the dangers of roentgen diagnosis both to the patient and to the physician and technician. While the deleterious effects of radiation are detailed in the section on radiation therapy, the dangers of prolonged fluoroscopy and of prolonged exposure of the workers in this field are not clearly delineated.

In keeping with the record of the Year Book Publishers, the typography and particularly the illustrations are of the first order. The publishers are to be congratulated.



This is a book which should facilitate the undergraduate teaching of radiology and should be most valuable for the student himself. It will also be helpful to the graduate student in this specialty as a short survey of the field and to the general physician who is interested in familiarizing himself with the accomplishments of modern radiology.

**RADICAL SURGERY IN ADVANCED ABDOMINAL CANCER.** By ALEXANDER BRUNSCHWIG, M.D., Professor of Surgery, University of Chicago. A volume of 327 pages, with 118 illustrations. Published by the University of Chicago Press, Chicago, Ill., 1947. Price \$7.50.

Dr. Brunschwig is one of the leading exponents of a trend in surgery toward the performance of radical and extensive procedures in the presence of cancer, even though the prognosis for ultimate survival is admittedly poor. His book is a report of 100 consecutive cases of abdominal carcinoma, with extension and/or metastasis to the extent that they could reasonably be considered inoperable. All were treated by what the author terms "massive resection."

The unsuccessful cases are given as much prominence as the good ones, so that the reader can form his own opinion of the value of this kind of radical surgery. The immediate operative mortality was 34 per cent, and 17 per cent of the patients received no palliation. The other half were benefited, since 30 per cent received palliation and 19 per cent had a prolonged survival time. Of the latter, 13 per cent were living and well, an average of forty months after the operation.

Some examples of operations are: removal of the entire stomach, spleen, transverse colon, and body and tail of the pancreas for carcinoma of the stomach; removal of the right half of the colon, distal half of the stomach, and periumbilical region of the abdominal wall for carcinoma of the colon; removal of all of the stomach, all of the pancreas, all of the

duodenum, spleen, omentum and left adrenal for carcinoma of the pancreas.

There are chapters on the history of cancer surgery, general considerations of operability, and the supportive treatment which is necessary in conjunction with radical surgery. The importance of adequate blood replacement is adequately stressed; it was not unusual for 2 or 3 liters of blood to be given while the patient was on the table.

The book is illustrated by clear photographs of the resected specimens and attractive diagrams which show what was done.

**CONFRONTATIONS RADIO-ANATOMO-CLINIQUES.** Published under the direction of M. CHIRAY, R. A. GUTMANN, AND J. SÉNÈQUE. Fascicule I. A volume of 56 pages, with 98 figures. Published by Masson & Cie, Editeurs, Paris, 1946. Price 370 fr.

Thirty reports of cases, beautifully illustrated, make up this first issue of a new French publication. The object, as set forth in the Introduction, is not to duplicate the radiologic atlas or the specialized review, but rather to serve as a reflection of the "hasards de la clinique." The plan is to present individual cases, both classical and atypical, along with the films which have made possible a diagnosis or—what may sometimes be even more useful—have led to an erroneous conclusion. Where desirable, photographs of operative specimens and histologic preparations will also be included.

The reports come from the monthly meetings organized under the direction of the editors, in the service of one of them. For that reason, gastroenterology is predominantly represented, but other fields will be considered in subsequent issues. If these carry out the promise of this initial number, the publication will easily rank among the most attractive of the post-war period and fulfill the hope expressed by the editors that it may constitute "un ensemble digne de l'Ecole Française."



## RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

*Editor's Note:* Secretaries of state and local radiological societies are requested to cooperate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates. Address: Howard P. Doub, M.D., The Henry Ford Hospital, Detroit 2, Mich.

### UNITED STATES

**RADIOLOGICAL SOCIETY OF NORTH AMERICA.** *Secretary-Treasurer*, Donald S. Childs, M.D., 607 Medical Arts Bldg., Syracuse 2, N. Y.

**AMERICAN RADIUM SOCIETY.** *Secretary*, Hugh F. Hare, M.D., 605 Commonwealth Ave., Boston 15, Mass.

**AMERICAN ROENTGEN RAY SOCIETY.** *Secretary*, Harold Dabney Kerr, M.D., Iowa City, Iowa.

**AMERICAN COLLEGE OF RADIOLOGY.** *Secretary*, Mac F. Cahal, 20 N. Wacker Dr., Chicago 6, Ill.

**SECTION ON RADIOLOGY, A. M. A.** *Secretary*, U. V. Portmann, M.D., Cleveland Clinic, Cleveland 6, Ohio.

#### Alabama

**ALABAMA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, John Day Peake, M.D., Mobile Infirmary, Mobile. Next meeting at the time and place of the Alabama State Medical Association meeting.

#### Arkansas

**ARKANSAS RADIOLOGICAL SOCIETY.** *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and annually at meeting of State Medical Society.

#### California

**CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY.** *Secretary*, D. R. MacColl, M.D., 2007 Wilshire Blvd., Los Angeles 5.

**LOS ANGELES COUNTY MEDICAL ASSOCIATION, RADIOLOGICAL SECTION.** *Secretary*, Moris Horwitz, M.D., 2009 Wilshire Blvd., Los Angeles 5. Meets second Wednesday of each month at County Society Bldg.

**PACIFIC ROENTGEN SOCIETY.** *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with State Medical Association.

**SAN DIEGO ROENTGEN SOCIETY.** *Secretary*, R. F. Niehaus, M.D., 1831 Fourth Ave., San Diego. Meets first Wednesday of each month.

**X-RAY STUDY CLUB OF SAN FRANCISCO.** *Secretary*, Ivan J. Miller, M.D., 2000 Van Ness Ave. Meets monthly on the third Thursday at 7:45 P.M., January to June at Lane Hall, Stanford University Hospital, and July to December at Toland Hall, University of California Hospital.

#### Colorado

**DENVER RADIOLOGICAL CLUB.** *Secretary*, Washington C. Huyler, M.D., Mercy Hospital, 1619 Milwaukee, Denver 6. Meets third Friday of each month, at the Colorado School of Medicine and Hospitals.

#### Connecticut

**CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary*, Robert M. Lowman, M.D., Grace-New Haven Hospital, Grace Unit, New Haven. Meetings bimonthly, second Thursday.

#### Florida

**FLORIDA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Maxey Dell, Jr., M.D., 333 West Main St., S. Gainesville.

#### Georgia

**GEORGIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Robert Drane, M.D., De Renne Apartments, Savannah. Meets in November and at the annual meeting of State Medical Association.

#### Illinois

**CHICAGO ROENTGEN SOCIETY.** *Secretary*, T. J. Wachowski, M.D., 310 Ellis Ave., Wheaton. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April, at 8:00 P.M.

**ILLINOIS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly as announced.

**ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary*, Frank S. Hussey, M.D., 250 East Superior St., Chicago 11.

#### Indiana

**INDIANA ROENTGEN SOCIETY.** *Secretary-Treasurer*, J. A. Campbell, M.D., Indiana University Hospitals, Indianapolis 7. Annual meeting in May.

#### Iowa

**IOWA X-RAY CLUB.** *Secretary*, Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of State Medical Society.

#### Kentucky

**KENTUCKY RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Sydney E. Johnson, M.D., 101 W. Chestnut St., Louisville.

**LOUISVILLE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Everett L. Pirkey, Louisville General Hospital, Louisville 2. Meets second Friday of each month at Louisville General Hospital.

#### Louisiana

**LOUISIANA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Johnson R. Anderson, M.D., No. Louisiana Sanitarium, Shreveport. Meets with State Medical Society.

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets first Tuesday of each month.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday, 7:30 P.M.

#### Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary*, Charles N. Davidson, M.D., 101 West Read St., Baltimore 1.

#### Michigan

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary-Treasurer*, E. R. Witwer, M.D., Harper Hospital, Detroit 1. Meetings first Thursday of each month from October to May, at Wayne County Medical Society club rooms.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS. *Secretary-Treasurer*, R. B. MacDuff, M.D., 220 Genesee Bank Building, Flint 3.

#### Minnesota

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, C. N. Borman, M.D., 802 Medical Arts Bldg., Minneapolis 2. Regular meetings in the Spring and Fall.

#### Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, John W. Walker, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, Edwin C. Ernst, M.D., 100 Beaumont Medical Bldg. Meets on fourth Wednesday of each month, October to May.

#### Nebraska

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, O. A. Neely, M.D., 924 Sharp Building, Lincoln. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

#### New England

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, George Levene M.D., Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

#### New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary-Treasurer*, Albert C. Johnston, M.D., Elliot Community Hospital, Keene. Meetings quarterly in Concord.

#### New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, W. H. Seward, M.D., Orange Memorial Hospital,

Orange. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called.

#### New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC. *Secretary*, William J. Francis, M.D., East Rockaway, L. I.

BROOKLYN ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Abraham H. Levy, M.D., 1354 Carroll St., Bklyn. 13. Meets fourth Tuesday of every month, October to April.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meetings second Monday evening each month, October to May, inclusive.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary-Treasurer*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 10. Meetings in January, May, and October.

LONG ISLAND RADIOLOGICAL SOCIETY. *Secretary*, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

NEW YORK ROENTGEN SOCIETY. *Secretary*, Wm. Snow, M.D., 941 Park Ave., New York, 28.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary*, Murray P. George, M.D., 260 Crittenden Blvd., Rochester 7. Meets at Strong Memorial Hospital, third Monday, September through May.

#### North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary-Treasurer*, James E. Hemphill, M.D., Professional Bldg., Charlotte 2. Meets in May and October.

#### North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, Charles Heilman, M.D., 1338 Second St., N., Fargo.

#### Ohio

OHIO RADIOLOGICAL SOCIETY. *Secretary*, Henry Snow, M.D., 1061 Reibold Bldg., Dayton 2. Next meeting at annual meeting of the Ohio State Medical Association.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary*, Hugh A. Baldwin, M.D., 347 E. State St., Columbus.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George L. Sackett, M.D., 10515 Carnegie Ave., Cleveland 6. Meetings at 6:30 P.M. on fourth Monday, October to April, inclusive.

RADIOLOGICAL SOCIETY OF THE ACADEMY OF MEDICINE (Cincinnati Roentgenologists). *Secretary-Treasurer*, Samuel Brown, M.D., 707 Race St., Cincinnati 2. Meets third Tuesday of each month.

#### Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Peter M. Russo, M.D., 230 Osler Building, Oklahoma City. Meetings three times a year.

**Pennsylvania**

PENNSYLVANIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

PHILADELPHIA ROENTGEN RAY SOCIETY. *Secretary*, Calvin L. Stewart, M.D., Jefferson Hospital, Philadelphia 7. Meets first Thursday of each month at 8:00 P.M., from October to May in Thomson Hall, College of Physicians, 21 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY. *Secretary-Treasurer*, Lester M. J. Freedman, M.D., 415 Highland Bldg., Pittsburgh 6. Meets second Wednesday of each month at 6:30 P.M., October to May, inclusive.

**Rocky Mountain States**

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, A. M. Popma, M.D., 220 N. First St., Boise, Idaho.

**South Carolina**

SOUTH CAROLINA X-RAY SOCIETY. *Secretary-Treasurer*, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston 16.

**Tennessee**

MEMPHIS ROENTGEN CLUB. Meetings second Tuesday of each month at University Center.

TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meets annually with State Medical Society in April.

**Texas**

DALLAS-FORT WORTH ROENTGEN STUDY CLUB. *Secretary*, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth 2. Meetings on third Monday of each month, in Dallas in the odd months and in Fort Worth in the even months.

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**CUBA**

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA. Offices in Hospital Mercedes, Havana. Meets monthly.

**MEXICO**

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA. *General Secretary*, Dr. Dionisio Pérez Cosío, Marsella 11, México, D. F. Meetings first Monday of each month.



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## ROENTGEN DIAGNOSIS

### THE CHEST

**Discussion on the Stethoscope Versus X-Rays.** John Donnelly. *South. Med. & Surg.* 108: 248-249, August 1946.

In certain diseases of the chest such as bronchitis, dry pleurisy, bronchiectasis, and heart disease, the stethoscope is a superior diagnostic instrument, but in the vast majority of chest conditions the x-ray examination is more informative. The author believes that most of the errors in radiologic diagnosis of chest diseases are due to inadequate use of available facilities and dependence on a single film. He urges more use of roentgen studies of the chest in the early years of medical training and believes they would contribute inestimably to a better understanding of the anatomy and physiology of the heart and lungs. He advocates the taking of a careful history, study of physical signs, and then study of the chest roentgenogram, with interpretation of the findings in the light of previous knowledge of the individual patient. In the diagnosis and treatment of chest conditions, the history is of supreme importance and the radiological findings next, while the stethoscopic findings are frequently only an aid in correct interpretation of the shadows seen on the film.

BERNARD S. KALAYJIAN, M.D.

**A Simple and Practical Method of Obtaining Complete Bronchograms.** J. Karl Poppe. *Am. Rev. Tuberc.* 54: 104-110, August 1946.

The author describes his method for obtaining complete bronchograms of one or both lungs. Anesthesia is obtained by spraying the throat thoroughly with a 1.0 per cent pontocaine solution. The patient sits on a stretcher in front of the fluoroscope and the radiopaque oil is dripped over the back of the tongue, using a straight metal cannula attached to a 20-c.c. syringe; 10 to 12 c.c. of oil are sufficient for each side of the chest. The patient is tilted toward the side to be filled and, after the oil is instilled, is placed in a recumbent position, the foot of the stretcher being elevated to obtain filling of the upper lobe bronchi. A single posterior semi-oblique upright film is sufficient for visualizing each side of the chest. For successful bronchography it is essential that there be adequate anesthetization of the pharynx and trachea, that the instillation be controlled by fluoroscopy, and that there be a minimum of time between completion of the injection and the exposure of the films.

L. W. PAUL, M.D.

**Bronchography in Tuberculosis: A Clinical Study.** L. Bryce Boyer. *Am. Rev. Tuberc.* 54: 111-121, August 1946.

This report covers a series of 50 cases of pulmonary tuberculosis in which bronchography was performed. All degrees and types of the disease were represented. Four patients had purely exudative disease. One of these showed bronchial stenosis; in none was bronchiectasis found. Of 11 patients with fibro-exudative disease 3 presented bronchial narrowing alone and 3 dilatation only, while one displayed both conditions. Among 30 patients with fibroid tuberculosis, 2 showed only bronchial stenosis, 19 had bronchiectasis without bronchial obstruction, 6 had both conditions, and 3 had

neither complication. The opinion is favored that the development of bronchiectasis in these patients was the result of the fibrous pulmonary changes superimposed upon alterations of the bronchi caused by infection.

In no case was a harmful effect produced on the tuberculous disease by bronchography. It is felt, however, that the procedure is not worth while as a routine in pulmonary tuberculosis because: (1) it is well known from autopsy findings that fibroid tuberculosis is associated with bronchiectasis; (2) the contrast medium remains in the parenchyma and obscures succeeding roentgenographic changes; (3) rarely reactions occur. The primary use of the method lies in determining the source of a positive sputum when ordinary roentgenographic methods fail.

L. W. PAUL, M.D.

**Interlobar Empyema.** Joseph Levitin. *Am. J. Roentgenol.* 56: 156-162, August 1946.

The author reviews the problem of interlobar empyema from the standpoint of diagnosis, etiology, and treatment. The roentgen diagnosis of an interlobar effusion is made from appropriate postero-anterior and lateral views. The author does not favor the use of oblique views. Careful correlation with the history and physical findings is necessary to distinguish empyema from an aseptic effusion.

The causes of interlobar empyema are pneumonia, metastatic blood-borne or lymph-borne infection, direct trauma, lung abscess, and primary infection.

Treatment consists of surgical drainage of the interlobar empyema. Complete spontaneous evacuation of the encapsulated empyema is unusual.

H. H. WRIGHT, M.D.

**Roentgenological Manifestations of Primary Pulmonary Coccidioidomycosis.** Max Rakofsky and Thomas W. Knickerbocker. *Am. J. Roentgenol.* 56: 141-155, August 1946.

The roentgenologic features of primary coccidioidomycosis as seen in a study of 60 cases are presented.

Clinically, primary coccidioidomycosis is manifest as an upper respiratory or mild bronchopneumonic illness with cough, chest pain, fever, erythema nodosum, and positive pulmonary roentgen findings. Most patients make a complete recovery after a period of several weeks. In some cases a secondary stage follows, characterized by severe skin and bone lesions, in addition to the pulmonary lesion, with a mortality of about 50 per cent. The secondary form follows the primary form only as an endogenous reinfection.

Positive roentgen findings of pulmonary abnormality were found in 85 per cent of the 60 cases studied. These findings were grouped as follows:

1. Nodular lesion, single or multiple..... 22%
2. Peribronchial infiltration..... 22.5%
3. Confluent consolidations..... 20%
4. Hilar lymphadenopathy..... 24.5%
5. Pleural involvement..... 5%
6. Cavity formation..... 5%
7. Bilateral nodular (local) dissemination. 20%

The last-named group, including 12 cases, represented a rather severe and extensive form of pulmonary involvement as compared with the others. The roent-

gen examination showed a widespread distribution of nodular lesions throughout both lungs, individual nodules varying in size from 5 mm. to 2.5 cm. in diameter. This form of primary involvement may show gradual clearing or may progress to the granulomatous stage. Five case histories illustrating this severe form of primary coccidioidomycosis are presented. Two cases came to autopsy, and the pathological findings are presented. One was an example of a generalized fulminating miliary coccidioidomycosis superimposed upon the bilateral, multiple nodular primary form. The other case showed a combination of active tuberculosis and coccidioidomycosis.

H. H. WRIGHT, M.D.

**Pulmonary Actinomycosis Due to Actinomyces Asteroides.** Frederick W. Shaw, Rebecca A. Holt, and Edward S. Ray. *Virginia M. Monthly* 73: 362-368, August 1946.

A 34-year-old white woman had a hacking, productive cough associated with slight hemoptysis and left chest pain. A chest film showed minimal infiltrative lesions in both infraclavicular areas with a small amount of fluid at the left base, and a diagnosis of pulmonary tuberculosis was made. The patient was acutely ill, with a white cell count of 28,000 (77 per cent polymorphonuclears). Shortly after admission to a tuberculosis sanitarium, Actinomyces was isolated from the pleural fluid, but no tubercle bacilli were found either in the fluid or the sputum. Two months after admission an abscess developed in the right buttock, and from this also Actinomyces was isolated. The patient was then transferred to the Medical College of Virginia Hospital, from which this report comes. By this time, respiratory distress had developed, along with moderate cyanosis. A moderate leukocytosis persisted. A diagnostic aspiration showed the pleural fluid, originally serous, to have become frankly purulent, and surgical drainage was instituted. Shortly after this, penicillin was given and Actinomyces disappeared from the drainage, which gradually ceased. A left breast abscess also required drainage, but it is not stated whether or not the organism was isolated from the abscess. A persistent fever yielded to sulfadiazine, and the patient was discharged and eventually returned to work about eight months after admission. Some six months later it was necessary to excise a sinus tract from the right buttock because of a persistent serosanguineous discharge. The wound healed cleanly. A few months after this, a left empyema necessitatis ruptured spontaneously, from the drainage of which Actinomyces was isolated. Penicillin was given, and after a few weeks the empyema space was obliterated. Subsequently cholecystectomy was done and the gallbladder was found to contain stones and to be the seat of an inflammatory process. Following operation, penicillin was given in large dosage in the belief that this was indicated for the "cure" of actinomycosis, though no evidence is here presented that the infection was due to this cause. Two years and six months after her first hospital admission, the patient was asymptomatic and without evidence of disease. A chest film revealed a thickened pleura on the left with no apparent residual empyema.

The authors believe that this case, with a recurrence after a period of remission during which the infection must have remained dormant in the pleural cavity, suggests the necessity of a follow-up period of several

years before the final results of the different therapeutic measures can be evaluated.

A full discussion of the bacteriological and cultural identification of the Actinomycetes and their classification is given. J. E. WHITELEATHER, M.D.

**Pulmonary Filariasis.** Harold Rifkin and Theodore P. Eberhard. *Ann. Int. Med.* 25: 324-329, August 1946.

The authors cite a recent editorial in the *Naval Medical Bulletin* (54: 181, 1945) in which the statement is made that there is in filariasis a "pulmonic phase manifested by a prevalent morning cough, conspicuous in natives of endemic areas, which leads to a suspicion of widespread tuberculosis." In the literature available to them they could find no record of proved pulmonary filariasis or filarial pneumonia. They had, however, occasion to examine a native of a South Pacific island whose clinical picture suggested this possibility.

The patient was a 39-year-old civilian laborer, who complained of a hacking cough, blood-stained sputum, and night sweats of two years' duration, as well as fatigue and malaise. Dullness, diminished breath sounds, and moist râles were observed in the right half of the chest, anteriorly and posteriorly, and below the angle of the scapula on the left side posteriorly. There was no lymphadenopathy and no evidence of elephantiasis of the upper or lower extremities.

A chest film showed a soft, mottled, diffuse shadow of increased density fanning out from the left hilum into the lower lobe and covering the lung field from the border of the eighth rib downward. The shadow became less dense below and laterally, leaving the lung margins almost clear. A shadow of the same character, but occupying an irregular area about 5 cm. in diameter, was present in the mid zone of the right second anterior interspace. Six weeks later all of the shadows had regressed. The fluffy shadows of parenchymal infiltration had cleared, leaving in the left lower and right upper lobes fan-shaped zones of hard linear densities extending from the hila.

Microfilariae (*Wucheria bancrofti*) associated with many eosinophils were found in sputum concentrates, but no acid-fast bacilli, yeasts, fungi, or molds. Peripheral blood examination revealed a heavy microfilarial infestation, and a skin test gave a positive reaction to a titer of 1:8,000 and 1:16,000. These findings are believed to suggest an acute filarial reaction involving the bronchial lymphatics. It is further suggested that edema and eosinophilic infiltration of these lymphatics were responsible for the transitory pulmonary infiltrations demonstrated roentgenographically.

The presence of the microfilariae in the sputum can be explained on two bases: first, rupture of the alveolar capillaries with an outpouring of the organisms circulating in the blood stream into the alveoli; second, involvement of the larger bronchioles and bronchi in a generalized filarial infection, producing increased intraluminal tension with resultant filarial bronchorrhea.

STEPHEN N. TAGER, M.D.

**Organizing Hemothorax—A Clinical Entity.** Robert Tinkham Crowley. *Am. J. M. Sc.* 212: 241-250, August 1946.

Organizing hemothorax may be defined as a condition, usually produced by trauma to the thoracic cavity

or its contents, in which there exists within the pleural space a clot formed by the resultant hemorrhage, which subsequently undergoes progressive organization by the ingrowth of fibrous connective tissue from the adjacent pleural structures. Its significance has only recently been recognized, and the methods of diagnosis and treatment are largely developments of World War II.

The signs and symptoms of organizing hemothorax can be classified into 2 groups: (1) constitutional, resulting from body response to reaction within the pleura, and (2) localizing. The constitutional manifestations are indistinguishable from those incident to pleural reaction from liquid blood or infection in the pleura and are in general those incident to any inflammatory reaction. The localizing signs and symptoms are of considerably more significance. These arise in the main from pressure by the clot upon the lung and adjacent pleural structures, producing a lowered vital capacity, and vary in severity with the amount of involvement.

Clinical signs are essentially those of fluid in the chest, and roentgenography and aspiration are essential for differentiation. Postero-anterior and lateral films usually show a diffuse haziness over the whole or part of the affected side of the chest, with collapse of the lung of varying degrees. Air is commonly but not invariably present. The area of pulmonary collapse is frequently seen in the most dependent portion of the pleural cavity and affects the lower lobe. Early in the course of the hemothorax there may be, if sufficient fluid and air are present, widening of the intercostal spaces on the side of the lesion with a perceptible shift of the mediastinum to the opposite side. The fluid level, depending upon whether or not air is present, may or may not be sharply defined. As the process of organization proceeds, the fluid level tends to become diffuse and hazy, the interspace of the thoracic cage narrowed, and the mediastinum shifted back toward the affected side. The diaphragm on the involved side, in the later stages, is elevated above its normal position. Fluoroscopy will confirm a restriction of respiratory movement in the chest wall and particularly of the diaphragm. Lateral roentgenograms are of particular importance in determining the exact location and extent of the lesion. Serial x-ray studies, rarely more than a week apart, are essential in following the progress of the organizing hemothorax. Of particular diagnostic significance are failure to recover fluid blood upon repeated aspiration, or recovery of only small amounts containing macroscopic clots, and the presence of pyogenic organisms in the pleural aspirate.

The treatment of organizing hemothorax may be conservative or radical, the choice depending almost entirely upon the amount of anatomic and functional involvement. The technic of operation and special features of operative treatment are discussed. Atelectasis and empyema are the most frequent postoperative complications and must be guarded against.

A typical case of organizing hemothorax is presented, together with roentgenograms.

**Spontaneous Pneumothorax in the Newborn.** Edwin P. Scott and C. C. Rotondo. *Am. J. Dis. Child.* 72: 207-210, August 1946.

Although relatively rare, spontaneous pneumothorax of the newborn is probably more common than generally supposed. In this paper, the authors have reported

the sixth case on record of this condition in an infant delivered by cesarean section. The study is especially interesting in that trauma during delivery is generally believed to play a major role in the etiology.

Fever and dehydration developed on the fifth day of life. The infant became cyanotic, lethargic, and flaccid, and had a mild convulsion. Treatment consisted in the administration of oxygen in addition to the usual measures to combat dehydration and convulsions. The following day the temperature was normal but respirations were shallow. A roentgenogram showed a right pneumothorax. Five days later, this had completely cleared.

The authors believe that treatment in these cases should be conservative, aspiration being reserved for the more severe forms. The importance of roentgenography is stressed, as clinical signs and symptoms are not always prominent in the newborn.

M. WENDELL DIETZ, M.D.

**Mucocellular Papillary Adenocarcinoma of the Lung and Lobectomy.** Kermit E. Osserman and Harold Neuhof. *J. Thoracic Surg.* 15: 272-278, August 1946.

Mucocellular papillary adenocarcinoma of the lung is uncommon. A review of the literature reveals 19 cases, all of which were diagnosed at autopsy. This type of tumor has been described by various authors under many different names, as alveolar-cell tumor, primary cancer of the lung, adenoma, papillary gelatinous adenocarcinoma, alveolar epithelial cancer, multicentric alveolar carcinoma, adenomatosis, etc. Neuburger and Geever in an excellent review (*Arch. Path.* 33: 551, 1942) classified all these types as alveolar-cell tumor of the lung, whether or not they are mucus-producing.

The tumor arises either as a multicentric nodular neoplasm or as a diffuse infiltrating growth; combinations of both types are occasionally observed. The diffuse form is characterized by involvement of a lobe or an entire lung on one or both sides. Metastases are not a prominent feature.

The microscopic picture of the nodular and diffuse forms is identical, and Malassez' description in 1876 adequately describes the histology. The tumor stroma is made up of the alveolar walls. The latter are lined by cuboid or columnar neoplastic cells in one or more layers. Papillary protrusions of such cells are frequent. Mucinous secretion is present.

A study of the clinical records revealed no distinctive symptoms. In some cases a diagnosis of pulmonary tuberculosis was made; in others, the course was rapid and the impression was one of lobar or bronchial pneumonia. The majority of the patients did not survive more than one year. Occasional symptoms are cough, hemoptysis, cyanosis, and pain in the chest with evidence of pleural effusion.

Three cases are presented. One case, reported in detail, was unusual in that symptoms were of three years' duration before the patient came to the authors' attention, and that, two years after lobectomy, there had been no evidence of recurrence. Roentgenograms showed a solid tumor occupying two-thirds of the left lower lobe. Two other cases recognized postmortem are mentioned briefly. HAROLD O. PETERSON, M.D.

**Scleredema: A Systemic Disease.** Bert L. Vallee. *New England J. Med.* 235: 207-213, Aug. 15, 1946.

Four cases of scleredema are presented, bringing the total to 103. This disease is characterized by firm, non-

pitting edema, affecting usually the face, neck, scalp, conjunctivae, and thorax, occasionally the arms, and more rarely the legs, sparing the hands and feet. The condition is not primarily of radiologic interest; x-ray examination of the chest has only rarely been carried out and usually shows no abnormality. One of the author's patients, however, had a right pleural effusion when first seen, and later a loculated effusion along the right border of the heart. Both these effusions regressed as the process cleared. Another of the patients had massive bilateral effusions during the initial phase of the disease. These are thought to be the first cases in which pleural and pericardial effusions have been reported as part of the scleredema syndrome. Such intrathoracic effusions are believed to be intrinsic features of the disease and indicate, as do the reported hydrarthroses, that scleredema is not limited to the skin and subcutaneous tissue and may, in fact, present a puzzling picture to the internist.

**Dextrocardia and Bronchiectasis. A Review of the Literature and a Report of Two Cases.** A. H. Russakoff and Harvey W. Katz. *New England J. Med.* 235: 253-255, Aug. 22, 1946.

With the present report of two examples, the total number of cases of dextrocardia complicated by bronchiectasis is brought to 50. The combination of sinus disease, bronchiectasis, and visceral transposition has been known as "Kartagener's triad." The dextrocardia is offered as proof of the congenital origin of bronchiectasis.

The incidence of bronchiectasis in the general population is estimated at less than 0.5 per cent, while the incidence of bronchiectasis in dextrocardia is about 16 per cent. With mass chest radiography cases of dextrocardia are bound to be discovered, and the author believes that a diligent investigation of these patients will show bronchiectasis and other abnormalities.

JOHN B. MCANENY, M.D.

**Demonstration of Ventricular Septal Defect by Means of Right Heart Catheterization.** Eleanor deF. Baldwin, Lucille V. Moore, and Robert P. Noble, with Technical Assistance of Michaelen Patterson and Doris M. Harnsberger. *Am. Heart J.* 32: 152-162, August 1946.

The recently developed technic for catheterization of the right heart has been found especially useful for the detection of interventricular septal defects. Following the introduction of the catheter, under fluoroscopic control, samples of blood may be withdrawn from various known areas. A comparison of the respiratory gas content of the various blood samples with one another and with that of arterial blood will indicate whether or not an arteriovenous shunt is present. Further information on the hemodynamics may be obtained by connecting the intracardiac catheter to a recording type of manometer and analyzing the resultant pressure tracings. Finally, by direct observation of the movements of the catheter within the right heart, useful impressions as to the size, shape, and location of the chambers of the heart may be acquired, which supplement the information obtained from the routine x-ray and fluoroscopic studies.

The demonstration of arterialization of the right ventricular blood is proof of an interventricular arteriovenous shunt. A variation of oxygen content of more

than 2 volumes per cent between ventricular and auricular samples may be considered a significant difference, denoting an abnormal communication.

The authors report their observations on 2 cases of congestive circulatory failure of obscure etiology, in which arterialization of the right ventricular blood, demonstrable by cardiac catheterization, led to a diagnosis of ventricular septal defect.

The detection of an arteriovenous shunt by this method depends upon the tip of the catheter being bathed by a sufficiently large admixture of arterial blood during the collection of the blood sample to produce a significant auricular ventricular oxygen difference. Small shunts therefore may be missed.

The method of cardiac catheterization is not described in detail beyond the statement that the radiopaque catheter is passed through the median basilic vein into the thorax under fluoroscopic vision, and that the tip is manipulated into the desired position, but reference is made to the description of Courmand *et al.* (*J. Clin. Investigation* 24: 106, 1945). [For a recent account see Sosman: *Radiology* 48: 441, May 1947. Ed.]

HENRY K. TAYLOR, M.D.

**Hernia Pericardii.** A. Lincoln Brown and Sydney F. Thomas. *Am. J. Surg.* 72: 262-266, August 1946.

A case of hernia of the pericardial sac is presented which is believed to be the first lesion of this type proved by operation. The literature is reviewed, with mention of 40 cases collected by Cushing in 1937, all found post-mortem. The condition has been ascribed to (1) weakness of the wall of the pericardial sac, most likely to occur at points of entrance of vessels or nerves; (2) external traction due to some localized adhesive process which tents the sac wall. No favorite sites are described.

The case here recorded, in a young male, was an incidental finding on routine chest roentgenography. A smooth rounded mass was seen in the right cardiohepatic angle. At operation a thin-walled sac, 7.5 x 10 cm., was discovered in the right lateral wall of the pericardium. Pericardial fluid was seen to swish back and forth from the parent organ on systole. The sac was easily extirpated and the wall was found to be fibrous tissue lined with polyhedral cells having large pale nuclei.

Diagnostic roentgenologic aids were (1) kymography, showing pulsations even greater than those of the myocardium; (2) the Trendelenburg position, which completely obliterated the mass; (3) diagnostic pneumothorax, which facilitated the outlining of the mass preoperatively. EDWARD M. DEYOUNG, M.D.

## THE DIGESTIVE SYSTEM

**Further Experiences in the Surgical Treatment of Congenital Atresia of the Esophagus with Tracheo-esophageal Fistula.** Conrad R. Lam. *Surgery* 20: 174-179, August, 1946.

The author has previously reported 4 cases of atresia of the esophagus and tracheo-esophageal fistula treated surgically (*J. Pediat.* 27: 456, 1945. *Abst. In Radiology* 47: 307, 1946). One child died after an unsuccessful operation. In one of the others, an antethoracic esophagus has now been completed, and at the age of two and a half years the child is eating without difficulty. A summary of this case is included in the present paper, though the procedure employed is now considered inferior to direct anastomosis. The other



two infants, in whom direct anastomosis was done, are alive and well at sixteen and eighteen months. All 4 cases were of Vogt's type 3B, having an upper blind pouch and a fistula between the lower segment and the trachea.

Three new cases, also of type 3B, are here reported, in all of which direct anastomosis was attempted. In the first case, the diagnosis was established on the first day of life, and on the next day anastomosis was accomplished. On the sixth day there was leakage of formula from the drainage site in the operative wound and on the tenth day a gastrostomy was established. Within one month drainage ceased, feeding by mouth was resumed, and the gastrostomy was allowed to close. This child was in a normal state of nutrition at the age of ten months. The other 2 cases are of interest surgically because of technical failures. In one of these the patient died. In the other the attempt at direct anastomosis had to be abandoned in favor of a multiple-stage procedure. The final plastic procedures in this case had not been completed at the time of the report.

J. E. WHITELEATHER, M.D.

**Antral Gastritis and Spasm: Their Clinical and Surgical Significance.** James W. R. Rennie. *Ann. Surg.* 124: 402-409, August 1946.

In this paper the author emphasizes the difficulty and the importance of an accurate diagnosis of antral gastric disease. Antral spasm is best estimated by the radiologist by fluoroscopy and by serial films, which show constant contraction without derangement of the normal mucosal folds of the antrum. If the spasm is marked or persistent, the films may show elongation and narrowing of the antrum, a picture very similar to that of some cases of antral gastritis.

A fluoroscopic diagnosis of antral gastritis can be made in the presence of a deranged antral systole coupled with the finding of stiff, unnatural folds which cannot be obliterated during pressure. The films characteristically show persistent spasm with elongation and a funnel-shaped narrowing of the antrum. Sometimes there is indentation of the duodenal cap. This is believed to be due to squeezing of the stiffened mucosa through the pyloric ring (Kirklin's sign).

The symptomatology of antral spasm and gastritis shows an amazing similarity. The findings are a peculiar combination of those seen with gastric ulcer, gastric carcinoma, and gallbladder disease. Acidity tends to be normal or high in cases of gastritis, but the free acid is low or absent in antral spasm.

Surgically, the primary concern is with those cases showing an antral defect simulating carcinoma. Attention to mucosal relief patterns and gastroscopic examination will provide the diagnosis in many cases. If a definite diagnosis cannot be made after a short period of observation with repeated examinations, exploration is indicated.

Four typical cases are presented to illustrate the similarities of spasm, gastritis, and carcinoma.

M. WENDELL DIETZ, M.D.

**Regional Ileitis Involving the Ileum, Cecum, Ascending Colon, and Transverse Colon.** I. I. Cash, L. S. Pilcher, A. E. Rappoport, and W. A. Barker. *Ann. Int. Med.* 25: 351-362, August 1946.

So-called "regional ileitis" was originally believed to involve principally the terminal ileum in a chronic granulomatous process. Later it was observed that

other segments of bowel could be involved by a similar process, particularly the upper part of the ileum, the lower jejunum, and the proximal portion of the colon. Clinical features are the presence of anemia, diarrhea, abdominal pain, low-grade fever, and a mass in the right lower quadrant. No definite etiological factors have been determined, although acute bacillary dysentery has been suspected of having some etiological relationship.

The clinical diagnosis of granulomatous ileocolitis is based primarily on the roentgen findings. In the very early stage nothing more than irritability, localized spasm, and hypermotility of the involved segment (usually the terminal ileum) may be seen. As the disease progresses, this portion of the intestine becomes smooth, thickened and contracted, with narrowing of the lumen producing the typical "string sign." The normal mucosal pattern is obliterated, and ulceration of the mucosa of the involved segment may be demonstrated on spot pressure films. The margins of the diseased portion are slightly fuzzy and irregular as a result of ulceration. In the later stages, it is not unusual to observe marked constriction, sufficient to cause obstruction, associated with dilatation of the intestine proximal to the lesion, accompanied by the development of fistula. Roentgenologically, the involvement is often sharply demarcated. Though many believe a barium meal study is of greater value, no case should be subjected to operation without a barium enema.

From the roentgenologic standpoint, the differential diagnosis usually lies between regional ileitis and ileocecal tuberculosis. Primary enterocolic tuberculosis is relative rare. In the absence of pulmonary tuberculosis and with the inability to recover acid-fast organisms from the stool, intestinal tuberculosis can usually be excluded, although an occasional case cannot be distinguished from regional ileitis, except at operation. Neoplasm, appendiceal abscess and Meckel's diverticulitis should be considered, but the history and the roentgen-ray findings are usually sufficient to exclude these.

Clinically, the early symptoms closely resemble those of appendicitis, but in the later stages the resemblance is less striking. Amebic colitis, chronic bacillary dysentery, and ulcerative colitis must also be considered in the differential diagnosis. Amebic colitis usually will show typical small, discrete, punched-out ulcers in the lower bowel, with pus and blood in the stool, and the amebae may often be recovered from a warm stool specimen. Ulcerative colitis can usually be diagnosed by roentgen-ray and the sigmoidoscopic examination. The diagnosis of chronic bacillary dysentery depends on the isolation of the specific organism from the stool and rising serial serum agglutination titers.

The general consensus of opinion at present considers surgery the only satisfactory treatment of granulomatous ileocolitis. All of the diseased bowel and the diseased mesenteric nodes must be removed if a satisfactory result is to be obtained.

A case in a 22-year-old soldier is recorded. This is of interest primarily because of the widespread involvement of the intestinal tract, but also because, having been closely followed in Army hospitals for over a year, it illustrates graphically the classical picture of the onset and progress of the disease, with all its diagnostic and therapeutic trials and pitfalls.

The original x-ray studies, made elsewhere, would seem retrospectively to have warranted a diagnosis of



ileocolitis involving the terminal ileum, cecum, and perhaps other portions of the colon, but though the possibility was mentioned, a definite diagnosis was not made. When the authors saw the patient, about a month later, the most significant roentgen finding was a very smooth tubular appearance of the distal 8 cm. of the ileum, which was somewhat narrowed and showed loss of the normal mucosal pattern. The five-hour film of the gastro-intestinal series showed similar changes. The fluoroscopic examination at the same time demonstrated irritability of the terminal ileum and cecum. On the basis of these observations, a diagnosis of terminal ileitis with involvement of the cecum and ascending colon was established.

In spite of wide radical resection, extending 12 inches above the obviously diseased part of the ileum (confirmed by examination of the specimen) and several inches beyond the involved half of the transverse colon, symptoms reappeared within a few months and an exploratory operation was undertaken. This confirmed the roentgen diagnosis of recurrence in the terminal ileum and colon. Because of the extent of the process, further resection was not undertaken. The patient was treated by rest, ultraviolet radiation, and cod-liver oil with good immediate results, but within six months there were further symptoms, and roentgen studies in a civilian hospital showed evidence of progression of the disease to involve the remaining portion of the ileum.

STEPHEN N. TAGER, M.D.

**Spontaneous Pneumoperitoneum Without Peritonitis and Without Demonstrable Cause.** J. M. Mason, E. M. Mason, and K. F. Kesmodel. *South. M. J.* 39: 620-624, August 1946.

Spontaneous pneumoperitoneum is usually due to a ruptured viscus, the most frequent cause being perforation of the stomach or duodenum by a benign or malignant ulcer. Other causes are rupture of the appendix or of the small bowel from ulcer and rupture of the colon or rectum as a result of carcinoma. In such cases there is usually an associated peritonitis calling for prompt operation.

A review of the literature revealed only a few cases of proved spontaneous pneumothorax in which no peritonitis developed and for which no cause could be found. The entrance of air *via* the fallopian tubes has been suggested but this seems unlikely considering the pressure required in doing a Rubin test. European authors speak of a "pneumatosis cystoides intestinalis" in which subserous blebs on the intestine, presumably due to a parasite, may rupture with the release of air.

The authors report a case of massive spontaneous pneumoperitoneum studied by them without discovery of the cause. Follow-up films showed the air to have been absorbed. In studying these cases the first film should be a lateral view (horizontal rays) with the patient supine. After this, an anteroposterior or postero-anterior view can be taken. Frequently a film with the patient erect is unnecessary. FRANCIS F. HART, M.D.

#### THE MUSCULOSKELETAL SYSTEM

**Still's Disease (Atrophic Arthritis, Atrophic Rheumatoid Arthritis or Infectious Rheumatoid Arthritis).** William F. Burdick. *South. M. J.* 39: 626-630, August 1946.

The author discusses the incidence, etiology, symptomatology, and physical signs of atrophic rheumatoid

arthritis in children. The hereditary background and body habitus of the individual are emphasized. Several etiologic theories are mentioned but the author concludes that no causes are known at present, and that the disease is probably of infectious origin.

Pain is present early and often precedes swelling of the joints. The child may become fretful and irritable; fever is present in varying degrees; the skin is pale and there may be an erythematous or pigmented eruption. Subcutaneous fibrous nodules are found in 20 per cent of the cases. Generalized lymphadenopathy and splenomegaly are usually seen in young children.

The x-ray picture is characteristic. At first only the soft-tissue swelling is seen. Later, rarefaction of the bone is evident, especially in the epiphyses. As the disease progresses, the gradual destruction of cartilage and loss of bone substance are striking.

Treatment involves general and psychological care, and orthopedic measures from an early date to prevent crippling and, if ankylosis becomes inevitable, to insure an optimum physiological position.

Two cases are reported. PHILIP W. DORSEY, M.D.

**Pathogenesis of Charcot's Joint.** Percy J. Delano. *Am. J. Roentgenol.* 56: 189-200, August 1946.

Using an extensive review of the pertinent literature as a basis, the author discusses the pathogenesis of Charcot's joint. Charcot and others have believed in the existence of special trophic nerves, damage to which permitted development of the so-called neurotrophic joint. Volkmann, a contemporary of Charcot, and others since his time contend that the changes seen in neurotrophic arthropathy are brought about by repeated subclinical traumata occurring in an insensitive joint, and deny the existence of trophic nerves. The author adheres to the latter belief.

A case is recorded in which the patient has been paralyzed from the waist down for fifteen years, following fracture of the first lumbar vertebra in an automobile accident. Roentgen examination showed extensive irregular bony overgrowth and osteosclerosis, consistent with a joint neuropathy. The trauma in this instance is ascribed to repeated turning of the patient on his right side for nursing care. Pathological changes occurring in neurotrophic joints are discussed in detail. A full bibliography is appended. H. H. WRIGHT, M.D.

**Disseminated Reticuloendothelial Tumor of the Bone Marrow with Nodular Osteosclerosis.** Frank Windholz. *Arch. Path.* 42: 206-213, August 1946.

A case of primary disseminated nodular reticuloendothelial tumor of the bone marrow with neoplastic growth of both the reticular and the endothelial components of this cellular system is presented. Circumscribed bone formation was present in areas involved by the tumor. The newly formed bone tissue was mainly contributed by metaplasia of the collagenous and reticular stroma of the tumor itself.

The patient, a 60-year-old woman, entered the hospital because of hypertensive disease (blood pressure 200/120) of about a year's duration, accompanied by some weight loss. The heart was slightly enlarged; the liver and spleen were of normal size. No lymph nodes or masses were palpated. Excretory urography revealed no abnormalities of the urinary tract. Plain roentgenograms disclosed numerous rounded sclerotic densities of various sizes in the innominate bones, the

sacrum, the lumbar vertebrae, the ribs, and the calvarium. The fifth vertebra was entirely dense. The roentgen picture suggested osteoclastic tumor metastases or Hodgkin's disease with atypical skeletal distribution, and biopsy revealed the findings described above. The patient's condition steadily declined and she died with signs of congestive heart failure eight months after admission. Permission for autopsy was refused.

#### Pyogenic Infection of the Spinal Epidural Space.

Robert M. Rankin and Paul G. Flothow. West J. Surg. 54: 320-323, August 1946.

Two hundred and seventeen cases of pyogenic infection of the spinal epidural space were collected from the literature up to 1941. Since then, 8 additional cases have been recorded. The disease occurs in the wake of suppurative infection anywhere in the body and is seen at all ages. The bacteria invade the spinal canal by direct extension from a contiguous suppuration, such as a vertebral osteomyelitis, a decubitus, or cellulitis of the neck, or by metastasis via the blood or lymph channels. The condition practically never results from a leptomeningitis perforating the dura. The staphylococcus is usually the causative organism, and the infection is localized chiefly to the broad areas in the epidural space, in the mid-thoracic and the mid-lumbar regions.

The infection may be extremely fulminating and cause death in a matter of hours or may be chronic, producing progressive paralysis over a period of months or years. Damage to the underlying spinal cord is profound. It is believed to be due to thrombosis of intraspinal vessels and obliteration of the intraspinal lymph spaces as a result of the contiguous inflammatory process.

The clinical picture follows a regular pattern—severe intractable pain in the vertebral axis followed by radicular pains in the distribution of the involved segment. In about half of the cases, there is tenderness of the involved spines and there may be a localized swelling. A marked rigidity of the spine is present. Within a day or so symptoms of cord compression appear, with paralysis and loss of sensation below the lesion. The usual laboratory signs of infections are present. The spinal fluid shows increased protein, usually 100 to 300 mg., some pleocytosis, and abnormality of the gold curve. The Queckenstedt test almost invariably demonstrates a partial or complete subarachnoid block. In the chronic cases, the symptomatology and findings are identical, but the course is less fulminating, with little or no febrile reaction.

If the physical signs make one suspicious of an epidural inflammatory mass in the lower lumbar region, lumbar puncture should not be done, as a meningitis may result. In these cases, cisternal puncture and myelography will confirm the diagnosis. Radiologic evidence of destruction of the vertebrae themselves is the exception rather than the rule. Once the diagnosis has been established, immediate laminectomy is imperative. The over-all operative mortality is 33 per cent; of those who survive, 40 per cent have complete return of function.

The authors present a case in a woman of thirty-one, following a vertebral osteomyelitis subsequent to a tooth infection. An unusual feature of the case was the fact that roentgenograms showed progressive destruction of the left lateral and transverse processes of

the 4th, 5th, and 6th cervical vertebrae. A hemilaminectomy was performed, and the laminae of the 3d to the 6th cervical vertebrae were found to be involved by a destructive inflammatory process. The posterolateral aspect of the dura was encased in a tough, fibrous, densely adherent layer of scar tissue, which also encased the 4th, 5th, 6th, and 7th cervical nerves. There was no free pus. All the scar tissue was dissected off, but the dura was not opened. Though treatment was delayed, it was followed by complete functional recovery and practically complete healing of the partially destroyed vertebrae as demonstrated roentgenographically. BERNARD S. KALAYJIAN, M.D.

#### Multiple Fractures in the Long Bones of Infants Suffering from Chronic Subdural Hematoma. John Caffey. Am. J. Roentgenol. 56: 163-173, August 1946.

Six cases of chronic subdural hematoma in infants are presented, in which 23 fractures and 4 contusions of the long bones were demonstrated. In none of the cases was there a history of injury to which the skeletal lesions could reasonably be attributed, and in none was there evidence of generalized or localized skeletal disease which would predispose to pathological fracture. Fractures of all of the large bones in the upper and lower extremities were included, but there were no fractures of the small bones of the hands or feet, and none of the cranium or flat bones of the pelvis and shoulder girdle. In none of the cases was there clinical or roentgen evidence of vitamin-C deficiency or of other generalized disease. History of injury to the head was also lacking in all cases. Several of the fractures appeared many weeks or months after the first clinical manifestation of subdural hematoma. There was little evidence to indicate that convulsive seizures were responsible for the fractures. Their cause remains obscure.

The presence of unexplained fractures in the long bones of infants warrants investigation for subdural hematoma. Routine examination of the long bones in subdural hematoma is necessary for identification of fractures, because many of them are clinically silent.

H. H. WRIGHT, M.D.

#### Displacement of Medial Epicondyle of Humerus into the Elbow Joint. Frederick M. Smith. Ann. Surg. 124: 410-425, August 1946.

Twenty-one cases of separation of the medial epicondyle of the humerus are reported in this study of a common childhood injury. The paper deals with that type of separation in which there is complete avulsion of the epicondyle with its downward and lateral displacement and incarceration into the elbow joint. Each case was associated with a dislocation of both bones.

The condition is frequently missed even with adequate roentgenograms, either because the lesion is not watched for, or because the displaced epicondyle is mistaken for an ossification center of the trochlear epiphysis. In cases of doubt, films of the uninjured elbow in identical positions should be taken for comparison. If the patient is unable to extend the elbow fully, two anteroposterior views are recommended—one with the lower humerus lying flat on the film and the other with the upper portion of the forearm lying flat on the film.

In 15 cases of the author's series, treatment of the medial epicondyle *per se*, after extraction from the

joint and after reduction of the elbow joint, consisted in fixation to the medial condylar ridge by means of a suture of heavy silk passed through a drill hole in the ridge. In 1 case, in a boy of seventeen, fixation was by single stainless steel screw. In 5 cases the epicondyle was completely excised and the common tendon of origin of the flexor-pronator group of muscles was resutured to the medial condyle. From the point of view of function, the author concludes that it makes little difference whether the epicondyle is replaced or removed. Actually, late follow-up examinations show slight enlargement or irregularity of the replaced epicondyle, but this is seldom detected by the patient himself. After following his patients for more than three years, the author can report that all showed excellent to perfect results, with a single exception, in which only a fair to good result was obtained.

The proximity of the ulnar nerve, in its groove on the posterior surface of the epicondyle, explains the frequency with which ulnar palsy is seen following this type of injury. All patients in the present series with this complication recovered complete function of the nerve. Treatment consisted in injection of the nerve sheath with saline solution and replacement to its normal location or transposition to the anterior surface of the medial condyle. M. WENDELL DIETZ, M.D.

**Fractures of the Carpal Scaphoid Bone: An Analysis of Sixty-Six Cases.** Moss M. Bannerman. Arch. Surg. 53: 164-168, August 1946.

The correct treatment of fractures of the carpal scaphoid is adequate prolonged fixation. This treatment is often omitted because of failure of diagnosis. This, in turn, is usually due to the mildness of symptoms in the early stages. In the author's series of 66 cases, 42 per cent were not diagnosed at the time of injury; 7 per cent of the patients failed to report the injury for several weeks, while in the other 35 per cent the fracture was diagnosed as a sprain clinically, and either no roentgen examination was made or the fracture line was missed.

In view of the large number of misses, the author recommends the use of oblique views at 30- and 60-degree angles, in addition to the routine palmar and lateral projections. The clinical symptoms consist of persistent pain in the anatomic snuff-box, with weakness and increased pain after exertion. Swelling and moderate limitation of motion are less constant findings, but their presence is sufficient to warrant detailed examination of the wrist.

Treatment consists in complete and prolonged immobilization, and this may be employed even when long periods (up to ten months) have elapsed following the injury. The author prefers a skin-tight cast including the thumb and extending from the elbow to the distal palmar crease, with the wrist in moderate dorsiflexion and slight radial deviation. In 85 per cent of his cases this led to healing without arthritic changes. All fractures incurred less than six months before instituting treatment healed satisfactorily. The presence of traumatic osteoporosis (Preiser's disease) did not prevent union. Operative intervention was not instituted until after at least two months' immobilization, and was limited to 10 cases. Functional recovery was excellent in all cases seen and was surprisingly rapid. This is attributed in great part to the continuous use of the fingers in physical and occupational therapy during the immobilization period. LEWIS G. JACOBS, M.D.

**Incipient Epiphyseolsthesis of the Hip. Its Diagnosis and Treatment.** Samuel Kleinberg. Am. J. Surg. 72: 190-201, August 1946.

Attention is directed to slipping of the capital epiphysis in adolescence as a cause of arthritis of the hip joint in the adult, and the author advocates early fusion of the slipped epiphysis to the femoral neck to prevent the arthritic sequelae as well as to relieve the immediate symptoms. Incipient and acute cases respond best to this procedure. Moderate or severe slipping, with or without treatment, eventuates in a hip joint which is not nearly so satisfactory.

The roentgenologic diagnosis is made from antero-posterior and lateral films, both of which are mandatory. The capital epiphysis slips downward, backward, and inward on the femoral neck. Normally it projects a little beyond the superior border of the neck, forming a sort of "shoulder." This "shoulder" is reduced or obliterated in epiphyseolsthesis. The femoral head may also present a crescentic appearance rather than its normal hemispherical shape. In the lateral view the downward displacement of the head is more readily observed. The epiphyseal plate is usually thickened and irregular and directly beneath it in the femoral neck there may exist several areas of rarefaction and streaks of sclerosis.

That the fundamental lesion is in the epiphyseal plate is pointed out by the author. The real cause is not known but several possible contributing factors are discussed. Once slipping has begun, it is likely to progress, but in some cases mild slipping may not advance even without therapy. The condition usually occurs in early adolescence and is signified by pain and limp. Most movements of the limb are free except internal rotation, which is always limited. Other details of symptomatology are mentioned.

The aim of treatment is to eliminate the epiphyseal plate at the earliest possible moment when the femoral head and neck are in a normal or nearly normal relation. For this the author prefers simple drilling of the femoral neck with penetration of the drill 1/4 inch beyond the epiphyseal plate. Two drill holes are so directed with x-ray control, the drills are withdrawn and the wound closed. A long plaster spica is applied and left in place for three months, during which time the patient is kept in bed. X-ray check-up is then done and another spica applied for another period of three months, the patient being permitted the use of crutches. A Thomas leg brace is then worn for at least six months, after which time the capital epiphysis is usually found to be fused to the femoral neck. Physiotherapy is used during the brace-wearing interval. Four cases are well documented and have shown good fusion with no subsequent epiphyseolsthesis. Excellent reproductions of roentgenograms of these cases are included.

PAUL. W. EYLER, M.D.

**Intermuscular Lipoma of the Thigh with Roentgenologic Findings.** Harold E. Simon and Hyman R. Senturia. South. M. J. 39: 624-626, August 1946.

A lipoma of the anterior thigh is reported as presenting several unusual features including an intermuscular location, resemblance to muscle hernia, a possible etiologic relationship to mild trauma suffered eight years previously, and a preoperative roentgen diagnosis which was later proved by microscopic examination of the excised tumor.

The patient had a swelling on the anterior surface of

the left thigh and complained of weakness in the leg and aching, especially at night and after exercise. Roentgenograms revealed a circumscribed lobulated area of decreased density traversed by coarse trabeculations, a typical roentgen picture of lipoma. The mass was excised from its subfascial location between the vastus medius and intermedius muscles.

Lipomas are among the most frequently occurring tumors and develop in practically any structure of the body. Differential diagnosis includes muscle hernia, cysts, hemangiomas, bone tumors, sarcomas of muscle or bone, liposarcomas, dermoids with a high fat content, hernias which contain fatty tissue such as omentum, the fat of lipohemarthrosis, and cholesterol stones and accumulations.

A lipoma requires surgical removal. Correct pre-operative diagnosis, made possible roentgenographically, is highly important to insure proper treatment.

W. P. MARTIN, M.D.

### OBSTETRICS AND GYNECOLOGY

**Value and Limitations of Pelvioradiography in the Management of Dystocia with Special Reference to the Midpelvic Capacity.** Arthur Weinberg and Samuel J. Seadron. *Am. J. Obst. & Gynec.* 52: 255-263, August 1946.

The authors present a study of 500 consecutive cases referred for x-ray examination because of dystocia, either actual or feared. All cases were studied with particular reference to the evaluation of midpelvic contraction and dystocia. The following conclusions were drawn:

1. Provided a reliable technic of roentgen pelvimetry is used, there is very little difference in roentgen mensuration.
2. The sum of the anteroposterior and the transverse diameter in any given pelvic plane is a more reliable index of the pelvic capacity than a separate consideration of each.
3. If the inlet measurements total less than 23 cm. and/or the midpelvic measurements less than 14 cm., dystocia is to be expected.
4. Cephalometry and fetometry are too inaccurate to be of much importance in pelvioradiography.
5. The feto-pelvic ratio was arbitrarily decided by the use of the precision stereoscope, and not by volumetric comparisons, which were too often misleading.
6. The pelvic architecture played a part in influencing the outcome, the prognosis being progressively worse in the following order: gynecoid, anthropoid, platypelloid, and android.
7. Malposition influenced the prognosis unfavorably.
8. In breech presentations prognosis is based almost entirely on the pelvic measurements and architecture, and no trial of labor is advised. In no case where a vaginal delivery of a breech presentation was advised did such a delivery terminate with fetal mortality.
9. A correct prognosis was given in 97.8 per cent of the series.
10. Only 35 per cent of this series in which dystocia was feared required operative delivery. Sixty-five per cent were given a good prognosis, illustrating the conservative influence of pelvioradiography.
11. The limitations of pelvioradiography are confined to the difficulty in estimating the soft-tissue

factors, behavior of the cervix, character of the labor contractions, the skill of the obstetrician, and the age and previous history of the patient.

HUGH A. O'NEILL, M.D.

**Aspiration of Stomach Contents into the Lungs during Obstetric Anesthesia.** Curtis L. Mendelson. *Am. J. Obst. and Gynec.* 52: 191-204, August 1946.

An analysis was made of 44,916 pregnancies to determine the incidence of aspiration of gastric contents into the lungs during anesthesia. It was found to be 0.15 per cent. Two entirely different syndromes may follow such aspiration. Aspiration of solid food usually produces the well known picture of laryngeal or bronchial obstruction with massive atelectasis and the classical x-ray picture of homogeneous density with varying degrees of mediastinal shift. Aspiration of liquids produces an asthma-like syndrome with cyanosis, tachycardia, and dyspnea; there is no mediastinal shift, and chest films show numerous, soft, mottled increased densities. The above picture has been misinterpreted as bronchopneumonia, tuberculosis, fungous infection, and even metastasis. Progressive cardiac embarrassment and pulmonary edema may supervene, and the diagnosis may then be confused with cardiac failure.

Experiments on rabbits indicated that the aspirated hydrochloric acid produced bronchial spasm and peribronchial congestive and exudative reactions interfering with normal intrapulmonary circulation.

Bronchoscopy was of no help in the treatment of this syndrome. The author suggests the oral administration of warm saline solution prior to giving anesthesia, to bring on vomiting, to empty the stomach, and alkalize the stomach contents.

FRANCIS F. HART, M.D.

**Intrauterine Respiration of the Human Fetus.** M. Edward Davis and Edith L. Potter. *J. A. M. A.* 131: 1194-1201, Aug. 10, 1946.

Intrauterine respiratory activity begins in early pregnancy and is spasmodic, irregular, and shallow, but does not differ greatly from the extrauterine pattern. Intrauterine respiration is associated with circulation of amniotic fluid throughout the lungs, the major changes at birth being substitution of air for fluid and the development of a more sensitive respiratory system.

Twelve to 48 c.c. of amniotic fluid were withdrawn and replaced by thorotrast in two groups of patients: one made up of women in the first half of gestation in whom therapeutic termination of pregnancy was indicated, the other of women at or near term in whom cesarean section was anticipated. When the fetuses were delivered in seventeen to fifty-two hours, thorotrast was demonstrable in the lungs and gastro-intestinal tract roentgenographically, and histologic preparations from the first group revealed widespread distribution of thorium in bronchi and alveoli. When delivery was done thirty to sixty minutes following the instillation of thorotrast, none of the contrast substance was found in the lungs or gastro-intestinal tract. Thorotrast was present in the lungs of the youngest fetus, of approximately twelve weeks' gestation. Incidentally, this was the first time that complete gastro-intestinal tract activity was demonstrated in a fetus at so early a stage. The entire gastro-intestinal tract was visualized.



In the younger fetuses, lung shadows produced by thorotrast have a finely granular appearance. In the older ones, the shadows are coarsely granular and the general pattern of the lung can be seen. Thorium is concentrated in the lungs, the result of fluid absorption by the prealveolar and alveolar circulation. Much of the amniotic fluid which enters the lung escapes in this way; some of the aspirated fluid, of course, may escape back into the amniotic cavity.

Reproductions of x-rays and photomicrographs of lungs are included.

HERBERT D. WELSH, M.D.  
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### THE GENITO-URINARY SYSTEM

**Experiences with Intravenous Urography in a General Hospital in India.** Charles M. Norfleet, Jr., and Philip J. Hodes. *J. Urol.* 56: 259-265, August 1946.

In their experience in a General Hospital in India the authors made urographic studies of 410 American soldiers with urinary symptoms, using various contrast media—diodrast, pyelectan, and skiodan. Evidence of some abnormality was obtained in 184 cases. Renal anomalies (including 5 cases of renal ectopia) were found in 54 (13 per cent). Forty-three (10.5 per cent) had roentgen evidence of renal calculi, but the actual incidence was much higher, as in many instances the examination was made only after the calculi had been passed. Twenty-three patients (5.6 per cent) showed evidence of infection (tuberculosis in a single instance). In 31 cases (7.5 per cent) with clinical symptoms directing attention to the prostate and its neighboring structures, the urograms showed suggestive changes, chiefly involving the ureters. Among other findings were a single case of renal carcinoma, 4 ruptured kidneys, 11 cases of renal ptosis, 2 bladder neck obstructions, and 1 dilatation of the middle third of the right ureter associated with intensive urinary colic and hematuria in a patient who was relieved of his symptoms following the removal of an adjacent but normal appearing appendix.

The authors emphasize the value of tests for dye sensitivity. In each of their cases an oral test was used. Although no edema of the buccal mucosa was seen, there were 3 patients in whom swallowing of about 1 c.c. of the medium produced a sufficiently severe reaction to prohibit intravenous injection of the dye. Following injection of 2 c.c. of diodrast, one patient in whom the oral test had been negative suffered severe nausea, vomiting, and shock, but there were no fatalities. There were 2 instances of hives following diodrast injection, but these yielded promptly to adrenalin. Disturbing nausea and vomiting followed pyelectan from a rubber-stoppered bottle but the same patient tolerated without incident pyelectan from an ampule. Four patients receiving pyelectan had a sterile thrombophlebitis.

FREDERICK A. BAVENDAM, M.D.

**Renal Ectopia: Demonstration of Crossed Unfused Ectopia by Fluoroscopy.** Benjamin Resnick and John H. Clark. *J. Urol.* 56: 173-178, August 1946.

Five cases of renal ectopia, 4 congenital and 1 acquired, encountered in 364 consecutive pyelographic studies are reported. This is a much higher incidence than the 1 in 1,000 generally given in the literature. Congenital uncrossed or simple ectopia is unilateral,

usually involves the left kidney, and is the anomaly most commonly seen.

The generally accepted view is that congenital ectopia results from a persistence of the fetal vessels, interfering with normal ascent in fetal life, so that the kidney becomes arrested at some point below the normal position. It has been frequently noted that ectopias are especially common among fused kidneys, as the presence of the isthmus interferes with ascent. Why the classical horseshoe kidney may be found in the normal position is difficult to explain. The suggestion that man's erect posture is a factor in the development of renal ectopia is not considered very logical, as ascent of the kidney takes place during the second month of fetal life.

Ectopia may be symptomless, but in all of the authors' cases some symptoms were present, as pain, urgency, frequency, and nocturia.

The diagnostic impressions in the 5 cases recorded were as follows: (1) ectopic left kidney (pelvic), uncrossed; (2) crossed ectopia with fusion (fusion confirmed by fluoroscopy); (3) crossed unfused ectopia; (4) uncrossed, probably fused ectopia; (5) fused kidney with acquired left ectopia. The third case is of particular interest, as the x-ray film suggested fusion, but fluoroscopic examination revealed a change in the relative positions of the organs and made it possible to classify the condition as a crossed *unfused* ectopia.

PAUL R. NOBLE, M.D.

**Large Pyelogenic Cyst with Crossed Renal Ectopia.**

H. H. Lerner and A. I. Gazin. *J. Urol.* 56: 162-168, August 1946.

Renal ectopia is generally recorded as occurring approximately once in 1,000 cases. [Norfleet and Hodes and Resnick and Clark (see preceding abstracts) report a much higher incidence.] In a year the present authors saw 9 cases: 4 of simple unilateral (1 pelvic), 2 of simple bilateral, and 3 of crossed ectopia. In one of the cases of crossed ectopia there was an associated pyelogenic cyst, *i.e.*, a cyst having a communication with the renal pelvis by a minute channel or calyx.

The patient was a colored male aged 22 years with symptoms referable to the upper gastro-intestinal tract. Physical examination showed a large, tense, freely movable tumor of the abdomen extending from two inches above the umbilicus to two inches above the symphysis. It extended obliquely across the abdomen from the left upper quadrant to the right lower quadrant. X-ray examination indicated that the stomach and the distal half of the colon were displaced upward and to the right by the mass noted on physical examination. Intravenous and retrograde urography showed a left hydronephrotic kidney and slightly below it on the left side an ectopic right kidney, whose pelvis and calices were dilated and from whose superior calix there extended a large ovoid cystic tumor with a dye capacity of 700 c.c. The mass extended obliquely downward and to the right, accounting for the previously noted physical findings. Drainage through a ureteral catheter inserted in the right ureter upward as far as the right kidney pelvis caused the mass to disappear. It apparently represented a large pyelogenic cyst arising from the upper pole of a crossed hydronephrotic ectopic right kidney and communicating with its pelvis by means of the superior calix. No note is made of operation or of clinical follow-up.

MARLYN W. MILLER, M.B.



**Supernumerary Kidney as a Cause of Uretero-pelvic Obstruction.** Hjalmar E. Carlson. *J. Urol.* 56: 179-182, August 1946.

A case of supernumerary kidney is reported bringing the total number of recorded cases to forty-seven. Supernumerary kidneys are usually located below the normal kidney, are smaller, exhibit depressed function, and are subject to ptosis, stone, and pyonephrosis. The supernumerary kidney is more often diseased

than the normal. If diseased, it should be removed, as its poor function renders it of doubtful value. In the case reported, the supernumerary kidney was located beneath the ureteropelvic junction of the left kidney and had apparently produced obstruction resulting in a calculous pyonephrosis which had destroyed the normally situated kidney. The presence of the supernumerary organ was discovered only at operation.

PAUL R. NOBLE, M.D.

## RADIOTHERAPY

**Combined Roentgen Radiation and Surgical Treatment of Large Benign Giant Cell Tumors of Bone.** G. Edmund Haggart and Hugh F. Hare. *Ann. Surg.* 124: 228-244, August 1946.

There are two schools of thought concerning the treatment of benign giant-cell tumors of bone. One cautions against the combined use of radiation and surgery on the basis that the radiation will damage the reparative processes. The other contends that the two therapeutic procedures should be employed in each case. The present paper reports the results obtained in 7 cases treated first with roentgen rays, then surgically curetted.

In each case there has been complete recovery with no evidence of recurrence of the tumor and no evidence of impairment of reparative processes. In all cases the bone tumor was irradiated through two portals, using 200 kv.p., 1 mm. Cu, at 50 cm. T.S.D. The portals were large enough to cover the lesion. Each portal received 900 r measured in air. It was noted at the time of operation that the tumors were less vascular and were more easily curetted than in similar cases not receiving preoperative irradiation.

[This series has been followed for an average of only 4.7 years. In a paper delivered to the Philadelphia Roentgen Ray Society on Feb. 6, 1947 (to be published shortly), Dr. Bradley Coley, of Memorial Hospital, New York, warned of malignant change occurring after fifteen to twenty years. He advised against combining roentgen and surgical therapy except in rare instances.]

STANLEY H. MACHT, M.D.

**Epithelioma of the Anus.** Harold D. Harvey. *Ann. Surg.* 124: 245-251, August 1946.

The author presents a review of 37 cases of epithelioma of the anus seen at the Presbyterian Hospital (New York). The sex incidence was nearly equal. Over one-fifth of the patients were less than forty years old. The study was undertaken to clarify the rationale for the choice of one or more of the various possible forms of treatment. Of the 37 cases, 15 are not considered because they received no treatment, or only palliative treatment. In 9, the treatment was considered unsatisfactory. Seven patients, all with extensive lesions, treated within the last three years are still alive. Six of these required abdominoperineal resection. The seventh was treated by radium needles.

Six patients have survived five years or more. Three of these had small tumors, approximately 2 cm. in diameter. In these the method of treatment was simple local excision for one, perineal proctectomy for the second, and excision biopsy followed by radium pack for the third. A fourth case was successfully

treated by perineal proctectomy. A fifth with a basal-squamous-cell type of epithelioma was successfully treated by interstitial radium needles, receiving a dose of 4,651 mg. hours. The sixth patient, with a tumor developing after irradiation for pruritus, lived twelve years before dying of the tumor.

The author concludes by stating that no one form of treatment is applicable to all, but that each patient must be considered as an individual problem. For large growths, or growths with metastases, a radical resection of the anus and rectum with removal of the inguinal nodes should offer the best chance of arrest. If radiotherapy is used, the field of irradiation should extend well above the gross upper limits of the tumor. Radiotherapy should usually be preceded by a temporary colostomy.

PAUL W. ROMAN, M.D.

**Sarcoma of the Vagina.** William K. Diehl and John S. Haught. *Am. J. Obst. & Gynec.* 52: 302-310, August 1946.

The authors report two cases of sarcoma of the vagina found in 8,589 gynecological admissions. Many of the vaginal sarcomas reported in the literature arise in childhood and are most commonly of the botryoid type. Adult sarcoma occurs in two forms, parietal and mucosal, the infiltrating parietal type being the more common.

These tumors are extremely malignant and are soon beyond the realm of favorable response to surgery and/or radiation. Surgery, electrosurgery, and radiation are the available means of treatment and are usually combined. Excision is most certainly indicated in the botryoid type, where the entire vagina is filled with grape-like clusters, but the procedure is sometimes difficult.

Since sarcomas in general are radiosensitive, vaginal sarcoma theoretically should respond if all the cells could be brought within the effective sphere of the rays. The base of the tumor must be adequately excised in order that it may be amenable to the application of a radium plaque. This plaque usually consists of 100 mg. of radium and is made to conform to the size and shape of the lesion. A large vaginal pack is used to maintain the plaque in its original position, at the same time distending the vagina and further protecting the bladder and rectum from the radium rays.

Roentgen therapy is often used as an adjunct to surgery and radium, and in these cases the total deep x-ray dosage depends upon local response. Treatment is given in divided doses through the usual pelvic portals.

Local recurrences of the growth should in general be treated in the same manner as the original lesion.

BERT H. MALONE, M.D.

**Malignant Testicular Neoplasms: Analysis of 80 Cases.** Reed M. Nesbit and Jack M. Lynn. Surgery 20: 273-279, August 1946.

A study of 80 cases of malignant disease of the testicles, none of which was followed for less than four years, has been made in an effort (1) to gain an estimate of the prognosis and to lay down criteria of an adequate follow-up, (2) to determine the significance of hormone assays, (3) to judge the efficacy of early treatment, and (4) to present trends in interpretation of material submitted to the pathologist.

The patients ranged in age from 2 to 66 years, the average being 35.7. Forty-eight of the tumors were in the right testicle, 28 in the left, 3 were bilateral and one was unspecified. The early clinical picture and history in 3 cases resembled acute epididymitis, and those handling testicular tumors are warned not to be misled into delaying orchietomy or hormone assays too long. Fifty-one of the cases showed no metastases at first examination; in the 29 who did, the retroperitoneal lymph nodes and lungs were most frequently involved. Subsequent to therapy of the areas of likely involvement, metastases appeared chiefly in the retroperitoneal lymph nodes, followed by the lungs, operative site, cervical lymph nodes, mediastinal lymph nodes, and bones, in that order.

Two patients of the present series having metastases clinically demonstrable were cured by deep x-ray therapy. One has been followed for 11.5 and one for 12.5 years, respectively, with no demonstrable recurrence. The first patient, 39 years old, had had a swelling in the scrotum for fifteen years. Several months before admission the mass began to grow larger and there was pain in the lumbar region of the back. Orchietomy was performed and the diagnosis was malignant teratoma of the testicle, chiefly large round-cell sarcoma. Three months after operation there was a large mass in the left upper quadrant but the chest and spine were negative roentgenographically. One series of deep x-ray therapy was given but the number of roentgens is not specified. At two and four months after operation, two series of x-ray treatments to the pelvis, abdomen, and chest, totalling 5,200 r each, were given.

The second patient, 52 years old, with a cryptorchid right testicle, was admitted with the history of swelling of the lower right side of the abdomen first noticed fifteen months previously. During the last three months, this had enlarged rapidly, and an infraumbilical mass the size of a grapefruit was present. Three preoperative deep x-ray treatments of 500 r each were given and the tumor was removed. At operation the cryptorchid testicle,  $6 \times 4 \times 4$  inches in size, and a large mass of metastatic retroperitoneal nodes were found. Both the testicle and the biopsied lymph node revealed large round-cell alveolar sarcoma. During the five months after operation, deep x-ray treatments totalling 2,600 r, were given. Twelve years later there was no evidence of recurrence.

With regard to hormone assay, analysis of the cases so studied shows 12 in which Aschheim-Zondek tests were done both before and after treatment. One negative test subsequently became positive, and one of low titer became significantly high. If the Aschheim-Zondek test is positive, the outlook is grave. Of 8 patients having hormone levels above 500 mouse units before treatment, only 2 are living, and all 8

with positive post-therapy determinations have died.

An analysis of the survivals as related to various factors of treatment was made. Five of 19 patients treated with simple orchietomy alone were alive at the time of the report, for an average of 9.3 years, but this figure is not statistically significant. Of 4 treated by orchietomy with both preoperative and postoperative irradiation, 2 were alive (average survival 12.1 years); of 17 receiving postoperative irradiation to the pelvis alone, 5 were alive (average 12.4 years). None of 23 given additional radiation after completion of the original program of treatment survived five years. The authors believe that malignant testicular tumors other than chorionepithelioma should have postoperative x-ray therapy to the pelvis and abdomen whether or not metastases can be demonstrated.

In regard to the elapsed time from appearance of symptoms, in a group of 10 whose treatment began within two months of onset of symptoms, and who had no demonstrable metastases, 6 patients or 60 per cent were living at an average of 9.3 years after treatment. Of 41 patients whose treatment was begun more than two months after onset of symptoms and who showed no demonstrable metastases, 13 or 31.9 per cent are living an average of 11 years after treatment. Statistically, the difference is not significant, but on the basis of reasoning alone, the authors advise therapy as early as possible. Preoperative x-ray therapy is not considered advisable for two reasons: (1) It makes necessary the leaving *in situ* of a malignant neoplasm which is known to metastasize early. (2) The possibility of incorrect diagnosis becomes stronger because x-ray therapy makes microscopic interpretation difficult. Figures from Memorial Hospital, however, where preoperative irradiation is used, show a higher percentage of five-year cures (29 per cent of 172 patients) than any other clinic in this country. This high level of success may be due to efficiency of the postoperative radiation rather than to the virtue of preoperative x-ray therapy, and more recent communications indicate that the Memorial Hospital group now favors orchietomy without preoperative irradiation.

Under present practice, at the University of Michigan Hospital, patients suspected of having neoplasms of the testicle are admitted to the ward at once, and orchietomy is performed the following day, after a sample of urine has been collected for hormone assay. The spermatic cord is exposed high in the scrotum, clamped and cut before any manipulation of the testicle is permitted. All patients receive postoperative x-ray therapy to the pelvis and abdomen, although the dosage is not specified.

Of the authors' entire series, 23.8 per cent are living an average of 11.1 years after treatment. Two of the 29 having metastases at the time of diagnosis were seemingly cured by x-ray therapy; 51 patients with no demonstrable metastases when first seen had a survival rate of 33.33 per cent.

Mention is made of the wide divergence of opinion among leading pathologists regarding grouping of testicular neoplasms. It is pointed out that once orchietomy has been carried out and adequate postoperative x-ray therapy has been given, the course cannot be altered by further therapy. Metastases occurring after the first adequate series of x-ray treatments have not been affected by further therapy.

J. E. WHITELEATHER, M.D.

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